DISSERTATION ON

MEAN PLATELET VOLUME:

A DIAGNOSTIC TOOL AND ITS IMPLICATIONS

IN

ACUTE CORONARY SYNDROME

Dissertation submitted to

THE TAMILNADU DR. M.G.R. MEDICAL UNIVERSITY

In partial fulfillment of the regulations
for the award of the degree of

M.D. DEGREE IN GENERAL MEDICINE

BRANCH – I

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THANJAVUR - 613 004

THE TAMILNADU DR. M.G.R. MEDICAL UNIVERSITY
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CERTIFICATE

This is to certify that this dissertation entitled 'MEAN PLATELET VOLUME: A DIAGNOSTIC TOOL AND ITS IMPLICATIONS IN ACUTE CORONARY SYNDROME'' is the bonafide original work of Dr.VIJITH PILLAI V.G in partial fulfilment of the requirements for M.D. Branch – I (General Medicine) Examination of the Tamilnadu Dr.M.G.R. Medical University to be held in APRIL - 2013. The period of the study was from April – 2012 to November - 2012.

Prof.Dr.S . MANOHARAN MD.,
Unit Chief M-4
Dept. Of Internal Medicine,
Thanjavur Medical College,
Thanjavur – 613004.

Prof.Dr.S.MUTHUKUMARAN. M.D.,
Head Of the Department,
Dept. Of Internal Medicine,
Thanjavur Medical College,
Thanjavur – 613004.

Prof. Dr.C. GUNASEKARAN. M.D.Dch,
DEAN in charge,
Thanjavur Medical College,
Thanjavur – 613 004.

DECLARATION

I, **Dr. VIJITH PILLAI V.G**, solemnly declare that dissertation titled **" DISSERTATION ON MEAN PLATELET VOLUME: A DIAGNOSTIC TOOL AND ITS IMPLICATION IN ACUTE CORONARY SYNDROME "**is a bonafide work done by me at Thanjavur Medical College, Thanjavur, during April - 2012 to November - 2012 under the guidance and supervision of **Prof.Dr.S.MANOHARAN, M.D.,** Unit Chief M-IV, Thanjavur Medical College, Thanjavur.

This dissertation is submitted to Tamilnadu Dr. M.G.R Medical University towards partial fulfilment of requirement for the award of **M.D. Degree (Branch - I) in General Medicine**.

Place: Thanjavur.
Date: 20-12-2012.

(Dr. VIJITH PILLAI V.G)
Postgraduate Student,
M.D. in General Medicine,
Thanjavur Medical College,
Thanjavur - 613 004.

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CONTENTS

Thanjavur Medical College

THANJAVUR, TAMILNADU, INDIA-613004

(Affiliated to the T.N Dr.MGR Medical University, Chennai)

ETHICAL COMMITTEE

CERTIFICATE

Name of the Candidate	: **Dr VIJITH PILLAI V.G**
Course	: **M.D., GENERAL MEDICINE**
Period of Study	: **April -2012 to November -2012**
College	: **THANJAVUR MEDICAL COLLEGE.**
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INTRODUCTION

Acute coronary syndromes are a spectrum of ischemic myocardial events that range from unstable angina to non- ST elevation MI and ST-elevation myocardial infarction. They have a common end result; acute myocardial ischemia which predisposes the heart to cardiac death and myonecrosis. Despite advances in diagnosis and management in recent years, acute coronary syndrome is still one of the most important cause of

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INTRODUCTION Acute coronary syndromes are a spectrum of ischemic myocardial events that range from unstable angina to non- ST elevation MI and ST-elevation myocardial infarction. They have a common end result; acute myocardial ischemia which predisposes the heart to cardiac death and myonecrosis. Despite the impressive strides in diagnosis and management in recent years, acute coronary syndrome (ACS) is still one of the most important cause of morbidity and mortality. Major risk factors implicated in coronary artery disease are mainly age, history of coronary artery disease in the family, cigarette smoking, systemic hypertension, LDL cholesterol, and diabetes mellitus. Apart from that,...

ABSTRACT

Introduction:

Platelets play an important role in the pathogenesis of atherosclerosis and coronary artery disease. Larger platelets are more active and facilitates the thrombus formation over the atherosclerotic plaque and subsequent acute coronary events. In this study an attempt is made to find out the significance of mean platelet volume in acute coronary syndrome.

Materials and Methods:

Study groups comprised of 111 subjects which included 45 patients with myocardial infarction , 41 patients with unstable angina and 25 control group. Blood sample was taken at the time of admission and sent for mean platelet volume analysis. Statistical analysis was made through"one way variance analysis(ANOVA)" , post-hoc Tukey HSD and bonferroni method. Association of MPV with selected risk factors of ACS was also studied along with short term outcome in MI.

Observations and Results:

MPV in MI group(9.84±0.67fl) was significantly higher when compared to Unstable angina (9.07±0.77fl) and control groups(6.85±0.73fl). MPV in Unstable angina group were also significantly higher when compared to control groups. MPV was significantly higher in hypertensives (9.42±1.03fl)when compared to non hypertensives(8.43±1.44fl). MPV was

found to be significantly higher in those with lower ejection fraction in MI groups. MPV was also significantly higher in those who died in MI groups(10.53±0.35fl). The sensitivity and specificity of MPV when compared to Trop t in detecting MI was 91.11% and 62.12% respectively and on ROC curve analysis 8.8fl was the cut off range .

Conclusions:

Mean platelet volume was found to be in the high normal range in those with acute coronary syndrome. It was found to predict the mortality and ejection fraction in MI. So MPV is a useful diagnostic tool in detecting acute coronary events and can predict the complications along with other parameters.

Key words:

Acute coronary syndrome, Mean platelet volume

Abbreviations: ACS- acute coronary syndrome, MPV- mean platelet volume, MI- myocardial infarction

INTRODUCTION

Acute coronary syndromes are a spectrum of ischemic myocardial events that range from unstable angina to non- ST elevation MI and ST-elevation myocardial infarction. They have a common end result; acute myocardial ischemia which predisposes the heart to cardiac death and myonecrosis. Despite the impressive strides in diagnosis and management in recent years, acute coronary syndrome (ACS) is still one of the most important cause of morbidity and mortality.

Major risk factors implicated in coronary artery disease are mainly age, history of coronary artery disease in the family, cigarette smoking, systemic hypertension, LDL cholesterol, and diabetes mellitus. Apart from that, various novel risk factors [16] have been identified like endothelial dysfunction, lipoprotein (a), homocysteine, and C-reactive protein. Delineation of risk factors [16] in coronary artery disease has a very significant role in its management .

In acute coronary syndrome, platelets have a major role in thrombus formation on the ruptured atherosclerotic plaque and consequent progression to myocardial infarction[12] . The role of platelets in acute myocardial infarction and developments of complications have been well established . Therefore platelet inhibitors like, acetyl salicylic acid, thienopyridine, and glycoprotein IIb/IIIa inhibitors, are used in the treatment of

acute coronary syndromes .The circulating platelet, at a time, in a person differ in size, density, and activity [4] . Alterations of these parameters may be associated with pulling the trigger of acute coronary syndrome and further complications [1]. The adhesive capability of large platelets are more and hence they tend to aggregate more than smaller ones [1]. Increase in size of platelets as implicated by platelet volume may contribute to increased tendency of thrombus formation on atherosclerotic plaque in acute coronary syndrome [2, 4]. This study, aims to investigate the association between mean platelet volume and acute coronary syndrome and its use as a diagnostic tool , in comparison with control group.

REVIEW OF LITERATURE

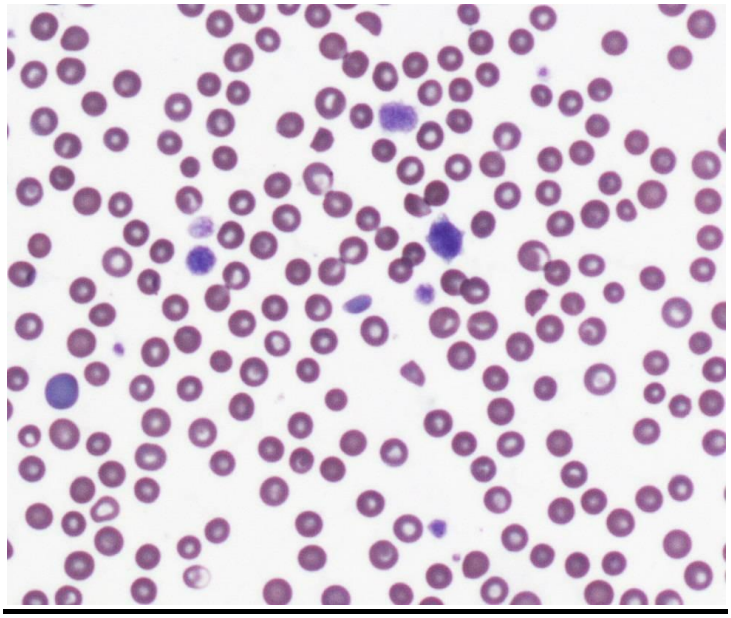
The role of platelets in acute myocardial infarction has been appreciated for several decades. Yet the last 5-10 years have seen a dramatic increase in the understanding, development, clinical evaluation and therapeutic application of platelet inhibitor therapy.

In 1841 Addison described platelets as "extremely minute granules" in clotting blood and the name "platelets" was assigned to it by Bizzozero. Their adhesive qualities as 'increased stickiness when a vascular wall is damaged' were also explained by him . Osler and by Hayem in the late nineteenth century identified platelets in microscopic examination of blood smear.

PLATELET STRUCTURAL AND FUNCTIONAL ANATOMY

Light Microscopy

On Wright-Giemsa stained blood smears, platelets appear as small anucleate, ovoid or round cells, with a pale grayish blue cytoplasm that contains homogenously distributed purple-red granules [50].



Platelet light microscopy

Dimensions

Platelets vary in number, size, density, age, and apparent physiologic effectiveness. The normal platelet count varies between 150 to 400,000 per µl, and normal platelet size (mean platelet volume) varies between 7.5 and 10.5 fl[50].

Electron Microscopy and Subcellular Organelles

By scanning electron microscopy, circulating resting blood platelets appear as flat discs with smooth contours, rare spiny filopodia , and random openings of a channel system, the surface-connected canalicular system (SCCS), which invaginates the platelet and is the conduit by which granule contents exocytose after stimulation [51]. Although the platelet is anucleate, transmission electron microscopy reveals a complex surface and a cytoplasm packed with a number of different subplatelet structures and organelles that are

essential to the maintenance of normal hemostasis

Glycocalyx

Structure: A glycocalyx, 15 to 20 nm thick, is visualized by transmission electron microscopy and contains glycoproteins, glycolipids, mucopolysaccharides, and adsorbed plasma proteins.

Function: The glycocalyx has a net negative surface charge due to sialic acid residues on the proteins and lipids; the charge is thought to minimize attachment of circulating platelets to each other . This structure is rich in carbohydrate moieties of membrane-associated glycoproteins, which serve as receptors to mediate transfer of signals by stimulatory agents. The glycocalyx interacts with platelet activators to facilitate platelet adhesion and aggregation.

Plasma Membrane

Structure: The platelet plasma membrane is a typical trilaminar membrane (20 nm thick)with glycoproteins, glycolipids, and cholesterol embedded in a phospholipid bilayer**.**

Function: The plasma membrane contains sodium and calcium ATPase pumps, which are important for maintaining ionic homeostasis. It has a specialized role in providing a surface for the acceleration of blood coagulation, in that a specific platelet coagulant protein, platelet factor 3, resides in this

lipoprotein-rich unit membrane.

Surface-connected Canalicular System

Structure: The surface-connected canaclicular system [52], also called the open canalicular system, weaves throughout the cell cytoplasm in a tortuous fashion.

Function: The functions of the surface- connected canalicular system[52] are to provide route of entry and egress for molecules, an internal reservoir of membrane to facilitate platelet spreading and filopodia formation after adhesion and a storage reservoir for membrane glycoproteins that increase on the platelet surface after activation.

Dense Tubular system

Structure: The dense tubular system is a closed-channel system consisting of narrow, membrane limited tubules approximately 40-60 nm in diameter. It contains amorphous, moderately electron-dense material resembling cytoplasm within its lumina. It is, infact, residual smooth endoplasmic reticulum from the megakaryocytes.

Function: This channel system is involved in the regulation of intracellular calcium transport because it has been reported to selectively bind,

sequester, and release divalent cations after activation. The dense tubular system is also the site of prostaglandin synthesis in platelets[53].

Cytoskeleton

General structure： The platelet cytoskeleton contains 30 to 50% of total platelet protein and is made up of three major structural components: an actin microfilament network present throughout the cytoplasm, a microtubule coil localized at the platelet periphery and a membrane skeleton comprising a network of short actin filaments that underlies the inner surface of the plasma membrane. Although they are distinct structures, interconnections between these elements are present.

Structure and Function of Specific Cytoskeletal Elements

Actin Microfilaments： Twenty to thirty percent of total platelet protein is made of actin (Pollard, 1990). Actin exists in two forms, G-actin (actin monomers) and F-actin (polymerized actin). In the unstimulated platelet, 30 to 40% of actin is polymerized into filaments; the balance of actin monomers are prevented from polymerizing by proteins such as profiling or thymosin B4 that sequester monomeric actin, or by proteins that cap filaments in the intact cell, such as gelsolin[54].

Upon platelet activation, the proportion of filamentous actin rapidly increases to

60-70%. Actin monomers polymerize onto filaments at platelet peripheries and bundles of new filaments form to fill developing filopodia.

Microtubules: A circumferential microtubule band that supports the discoid form of the platelet is made up of two non identical subunit proteins (Alpha and Beta tubulin) associated with microtubule associated proteins (MAPs). The 25 nm diameter microtubule coil lies adjacent to, but does not touch the plasma membrane. Microtubules are present primarily in their polymerized form in unstimulated platelets. Platelet activation results in microtubule disassembly, then reassembly; such alterations in the marginal microtubule bundle result in platelet shape changes[53].

Membrane Skeleton: The short actin filaments of the membrane skeleton, which underlie the inner surface of the plasma membrane, together with the microtubule coil, are thought to help stabilize the platelet discoid shape. Two major platelet membrane glycoproteins, GP IIb-IIIa and GP Ib-IX are associated with the membrane skeleton.

Granules

Platelets contain four distinct populations of granules: alpha granules, dense bodies, lysosomes, and microperoxisomes[50]. After platelet stimulation by agonists, granules fuse with channels of the surface-connected canalicular system and extrude their contents (White, 1974). Internal contraction is required for this extrusion and ultimate discharge into the surrounding medium.

α- Granules :

Structure: α Granules are the predominant granule type with a cross-sectional diameter of approximately 300 nm. The α granule has been subdivided morphologically into three distinct zones by electron microscopy: an electron-dense nucleoid that occupies the bulk of the granule, a peripheral zone of lower electron density that lies adjacent to the granule membrane and 1 to 6 tubular structures that reside in the electron lucent peripheral zone.

Content: β -thromboglobulin and platelet factor 4 have been localized to the dense nucleoid. Von Willebrand factor is present in the tubular structures of the granule peripheral zone. Thrombospondin, and fibrinogen are present in the granular matrix. Other proteins present in α granules include albumin, immunoglobulin G (IgG), fibronectin, platelet derived growth factor, GP IIb-IIIa, Beta amyloid protein precursor, factor V, multimerin, a factor V/Va binding protein, transforming growth factor β1 and a plasminogen activator similar to tissue plasminogen activator.

Proteins present on the α-granule membrane include P-selectin, GP IIb-IIIa, granule membrane protein-33 (GMP-33), CD9, platelet-endothelial cell adhesion molecule 1 (PECAM-1) and osteonectin.

Dense Bodies:

Structure: Ultrastructurally, dense granules have a bull's eye appearance. They are the most electron-dense organelles in platelets. With an approximate diameter of 250 nm, these granules contain a large reservoir of ADP, a critical agonist for platelet activation that amplifies the effect of other stimuli

Content: The principle constituents of dense granules are a non metabolic pool of adenosine nucleotides (adenosine triphosphate and diphosphate, ATP andADP), PPi, calcium and magnesium and serotonin (5-hydrotryptamine). In addition, dense bodies contain guanosine triphosphate and diphosphate (GTP and GDP). The dense granule membrane contains P-selectin and granulophysin.

Lysosomes:

Structure: Lysosomes are small, acidified vesicles, approximately 200 nm in diameter, that are identifiable only with specific cytochemical stains for acid phosphatase and aryl sulfatase or through immunocytochemistry for cathepsin D and lysosome-associated membrane proteins

Content: Lysosomes are the only platelet granules that contain acid hydrolases. Platelet lysosomes contain a large variety of enzymes, including

β hexosaminidase and β glycerophosphatase. Lysosomal membrane glycoprotein (LIMP-CD63) and lysosomal associated membrane proteins 1 and 2 (LAMP-1 and LAMP-2) become expressed on the plasma membrane after activation.

Microperoxisomes:

Structure: Microperoxisomes are small (90nm) granules that are relatively few in number in platelets and can be demonstrated only cytochemically.

Content: They are reactive with alkaline diaminobenzidine medium. The enzyme responsible for the cytochemical peroxidase activity in microperoxisomes is catalase.

Coated Vesicles:

Structure: Coated vesicles are 70 to 90 nm organelles

Content: The polyhedral coat on the surface of these vesicles is composed of clathrin. Plasma components are transported to platelet granules by coated pits and vesicles.

Mitochondria

Structure: Mitochondria in platelet are similar, with the exception of smaller size to those in other cell types. There are approximately seven per

human platelet.

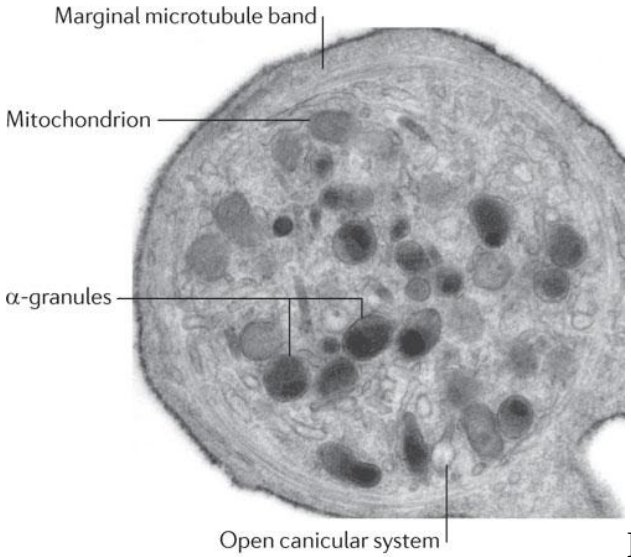
Content: Mitochondria are the site of activity for all components of the respiratory chain and for almost all enzymes in the citric acid cycle.

Glycogen

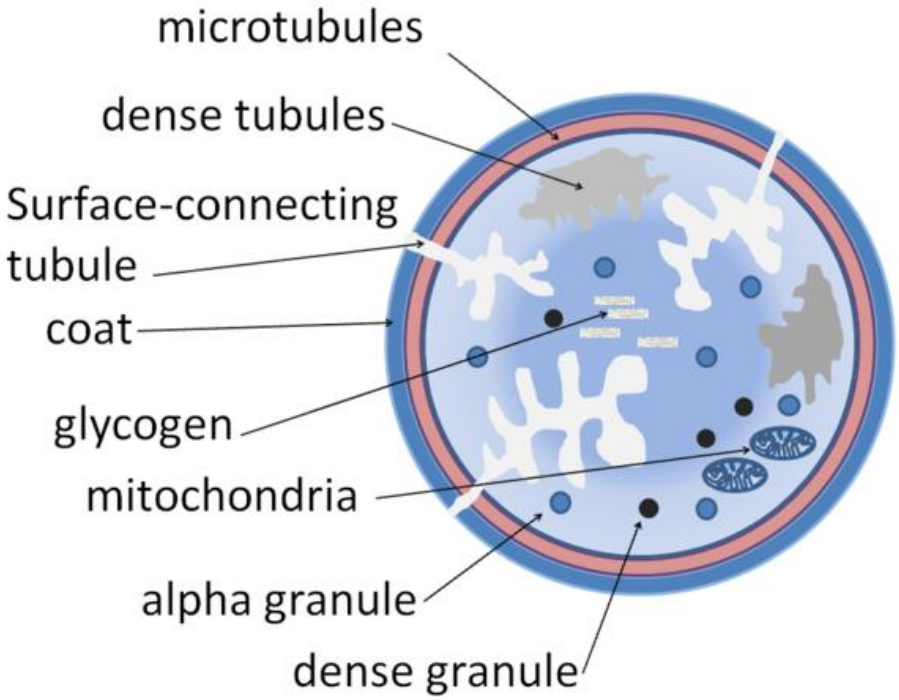
Platelets contain small particles of glycogen or masses of closely associated glycogen particles; these play an essential role in platelet metabolism.

PLATELET PHYSIOLOGY

A GLOBAL VIEW: The point of this "global view" is to emphasize a limited number of major current features of platelet physiology. To begin, it is fair to say that the platelet has come a long way from its past as an "inert particle" or possible artifact [55] to its present recognition as a remarkable fragment of megakaryocyte cytoplasm, capable of intense, focused activity that produces a tenacious mass at a site of vessel damage or disease . The clinical relevance of platelets is well illustrated by the widespread use of platelet gpIIb-IIIa antagonists (e.g., abciximab, eptifibatide) during angioplasty [56] and by the general acceptance of aspirin as an antiplatelet agent to prevent heart attack and stroke [57,58]



Electron microscopic view of platelets



(Diagram of a human platelet displaying its components)

Platelet Lipids and Proteins

Membrane Lipids

Phospholipids constitute 80% of the total platelet lipid, although smaller amounts of neutral lipids and glycolipids are also present. The five major phospholipids identified in human platelets are phosphatidylcholine, phosphatidylethanolamine, sphingomyelin, phosphatidylserine and phosphatidylinositol. Almost all platelet fatty acids are esterified in phospholipids, leaving only trace amounts of free fatty acids. Arachidonic acid, the precursor of prostaglandins and thromboxanes, is enriched in these phospholipids and the metabolism of arachidonic acid is critical for normal platelet function (Marcus, 1976). Neutral lipids make up approximately 28% of total platelet lipids, the predominant neutral lipid being cholesterol.

Membrane Glycoproteins

Platelet membrane glycoproteins mediate a wide number of adhesive cellular interactions. These glycoproteins function as receptors that can receive signals from outside the platelet, facilitating cell-cell interactions; binding of specific ligands to these receptors result in distinct platelet responses to the external environment**.**

Glycoprotein IIb-IIIa: Glycoprotein IIb-IIIa is the principal receptor on the platelet plasma membrane (Philips et al, 1988). It belongs to

the integrin family of proteins. A Ca^{2+} dependent conformational change in GP IIb-IIIa after platelet agonist induced stimulation facilitates strong binding to fibrinogen and VWF resulting in platelet aggregation**.**

Glycoprotein Ib-IX: Platelets interacts with VWF with the help of glycoprotein Ib receptors. GP Ib also functions as a binding site for thrombin. GP Ib is present on platelet surfaces in a 1:1 ratio with GP IX.

Other membrane Glycoproteins: Membrane glycoproteins GPIa-IIa, GPIc-IIa, helps in adhesion of platelet to collagen, laminin and fibronectin . GP V forms a non covalent complex with GP Ib-IX in the platelet membrane. PECAM-1 binds to heparin like molecules. GP IV is a receptor for thrombospondin. GP IV is also reported to bind collagen.

<u>Other Platelet Proteins</u>

Other proteins present in the platelet are platelet factor 4, β thromboglobulin, thrombospondin, platelet derived growth factor, fibronectin.

Platelet Factor 4 (PF4)**:** The anticoagulant activity of heparin is neutralized by binding with PF4. Other activities like, potentiation of platelet aggregation also mediated by PF4. Heparin administration can mobilize this endothelial-bound pool of PF4 into the circulation . PF4–heparin complexes and PF4 –heparin-like molecule complexes on endothelial cells have been

implicated as the target antigens in heparin-induced thrombocytopenia with thrombosis PF4 also binds to hepatocytes, which take up and catabolize PF4. PF4 is a weak neutrophil and fibroblast attractant. It inhibits angiogenesis, perhaps through inhibition of endothelial cell proliferation. Other functions of PF4 including histamine release from basophils, inhibition of tumor growth and megakaryocyte maturation, reversal of immunosuppression, enhancement of fibroblast attachment to substrata, potentiation of platelet aggregation

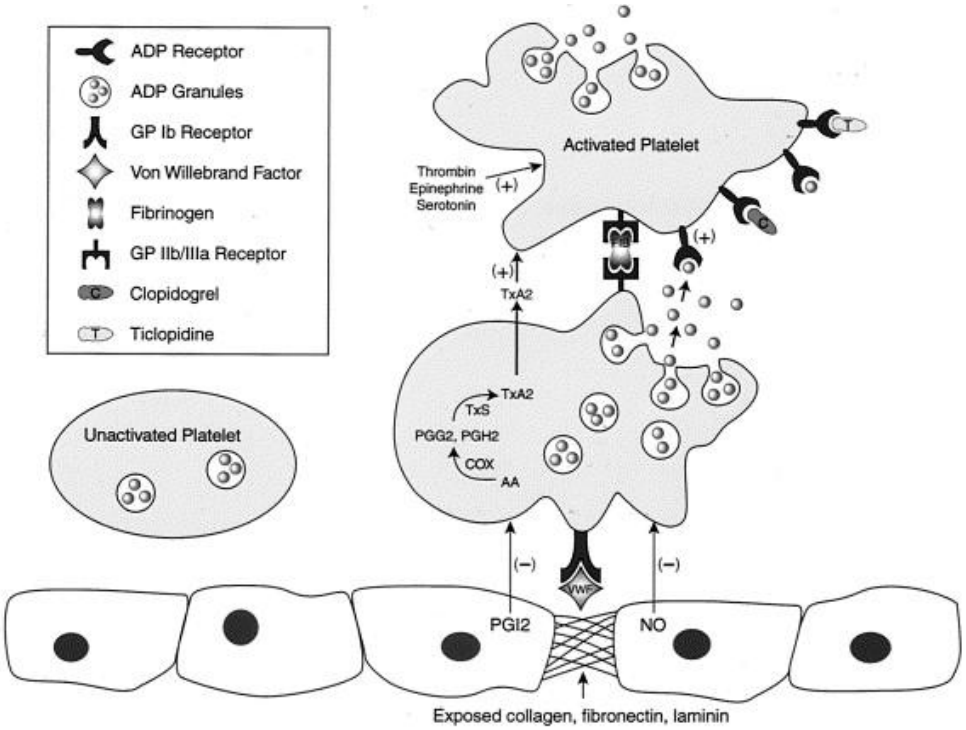


Diagram demonstrating the platelet adhesion and activation.

Activated platelets release dense platelet granules containing adenosine 5′diphosphate (ADP) and thromboxane A2 (TxA2) , which results in aggregation and activation of other platelets and thereby amplifying the effect.

Drugs such as clopidogrel (C) and ticlopidine (T), block ADP-receptor mediated platelet activation. Aspirin causes inhibition of cyclooxygenase (COX), thereby decreasing the synthesis of prostaglandins G2 and H2, which lead to reductions in production of thromboxane A2 (TxA2) by thromboxane synthase (TxS).

PLATELET BIOCHEMISTRY

The platelet has minimal ability to synthesize protein because it contains only low levels of RNA and lacks a nucleus. In terms of dry weight, the platelet is composed of approximately 60% protein, 15% lipid and 8% carbohydrate. Platelet minerals include magnesium, calcium, potassium and zinc. Platelets contain substantial amounts of vitamin B12, folic acid and ascorbic acid.

Platelet Energy Metabolism

There are several similarities between the energy metabolism of the platelet and that of skeletal muscle. Both involve active glycolysis and the synthesis and use of large amounts of glycogen and in both, the major mediator of intracellular energy use is an actinomysin-like adenosine triphosphate. The platelet, like muscle is metabolically adapted to expand large amounts of energy rapidly during aggregation, the release reaction and clot retraction.

The major energy source for the platelet is glucose, which is rapidly taken up from the plasma. Platelet energy is derived from the metabolism of glucose and

to a lesser extent from the metabolism of fatty acids. Energy is provided in approximately equal amounts by glycolysis and the citric acid cycle. Platelet energy reserve is provided by the metabolic pool of platelet nucleotides that is in a state of continuous turnover.

Nucleotide Metabolism

Adenine nucleotides constitute 90% of free platelet nucleotides and are partitioned into at least two different pools, which undergo minimal interchange. The metabolic or cytoplasmic pool makes up 40% of total adenine nucleotides; it is used for the maintenance of various energy consuming cell functions and is retained during platelet release.

The storage pool, which is present in the dense bodies, contains approximately two-thirds of the total platelet nucleotides, mainly in the form of ADP and ATP. It is metabolically inactive, does not rapidly incorporate exogenous adenine or phosphate, and equilibrates slowly with the metabolic pool. Nucleotides in this pool are extruded from the platelet during the release reaction and cannot be replenished after release. ATP hydrolysis is required for conversion of G-actin to F-actin. The ATP that is broken down to provide energy for the release reaction is not rephosphorylated, but rather is irreversibly degraded to hypoxanthine which diffuses out of the cell. Platelets also contain guanine nucleotides and uracil and cytosine pyrimidines.

Arachidonate Metabolism

Arachidonic acid is released from platelet membrane phospholipids after stimulation by numerous agonists through the enzyme action of phospholipase A2 or the combination of phospholipase C and diglyceride lipase. After release, arachidonic acid can be acted on by either lipoxygenase, which results in the production of peroxy and hydroxyl fatty acids, or by cyclooxygenase, which ultimately results in production of thromboxanes and prostaglandins.

Platelet "Coagulation" Factors

Numerous platelet proteins interact with plasma coagulation proteins although the mechanism by which platelet membrane component becomes reorganized and capable of functioning as a catalytic surface for plasma proteins are not known.

Several plasma coagulation factors are associated with platelets, including von Willebrand factor, coagulation inhibitors, and factor XIII.

Various substances associated with or derived from the platelet have been designated platelet factors 1 to 10 and denoted by Arabic numerals. The most important of these are PF4 and PF3.

Platelet Factor 3

PF3 is required in at least two steps in the process of blood coagulation,

namely the interaction between factors IXa and VIIIa, which results in the activation of factor X, as well as the interaction between factor Xa and factor Va which leads to the formation of prothrombinase. These coagulation reactions are greatly accelerated on the platelet surface.

PLATELET COUNT

The normal platelet count varies between 1,50,000-3,50,000/mm^3

PLATELET VOLUME

The normal mean platelet volume varies between 6 – 11 fl (wintrobes 12^{th} ed).

ORIGIN OF PLATELETS FROM MEGAKARYOCYTES

The megakaryocyte is a large hematopoietic cell, the cytoplasm of which fragments to form circulating blood platelets. The histogenesis of platelets from megakaryocytes was first described by James Wright in 1910. The megakaryocytes are sessile polyploid cells which in turn descend from diploid pluripotent hematopoietic stem cells of marrow. The megakaryocytes are imprisoned within the sub endothelial layer of marrow sinuses by their very girth and volume (average 5000 femto litres, Zhang YJ, 1991). In these marrow niches, mononuclear progenitors undergo diploid doublings by the unique process of endomitosis. Subsequently the polyploid megakaryocytes

accumulate a bulky compartmentalized cytoplasmic mass with large volumes that at end stage maturation disintegrates abruptly to yield between 1000 and 8000 platelets having a volume of 7-9 femto litres each (Martin et al, 1982; Stenberg and Levin, 1989;Corash, 1989). Megakaryocytes are suicidal microorgans whose mission is to proliferate and then fragment their cytoplasm on demand to maintain blood platelets at relatively steady levels of about 1,50,000-3,50,000/mm^3**.**

Maintenance of platelet counts within this range represents a surplus of over 10 times that is necessary to ensure routine haemostasis but provides a precautionary reserve for times of excess platelet loss or consumption.

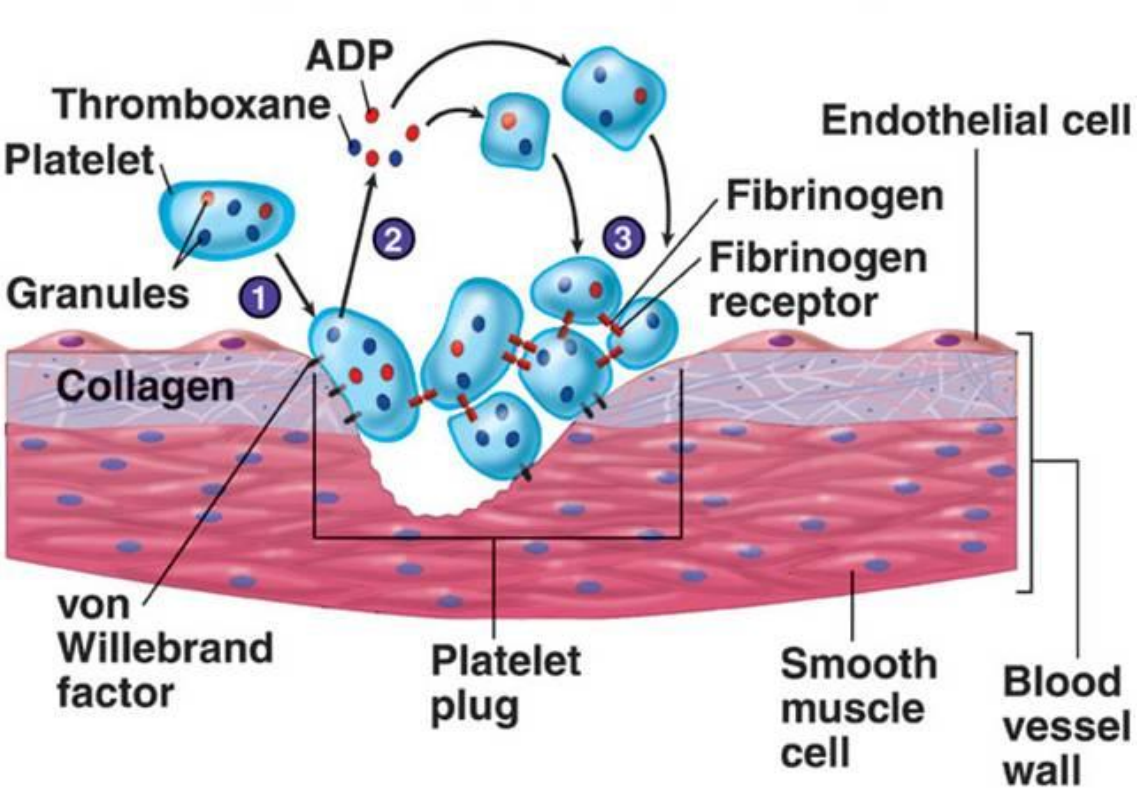
PLATELET LIFE SPAN, TURN OVER & REMOVAL

Platelet life span, based on the time required to clear labelled platelets from circulation, has been estimated to be 8-12 days in humans. The sites for platelet removal appear to be spleen, the liver and bone marrow. Degranulation and loss of density and platelet constituents has not been shown to decrease platelet life span indicating that the number of haemostatic interactions may not be a key component**.**

PLATELET ADHESION, ACTIVATION & AGGREGATION

The anti thrombotic properties of intact vascular endothelium include potent

platelet inhibitors. These inhibitors include PGI2, NO and CO which are labile molecules that are released by endothelial cells and act locally as autocoids and ADPase, an ectonucleotidase of endothelial membranes that breaks down platelet activating ADP.



Adhesion

On vascular intimal injury, the antiplatelet properties of endothelium are diminished locally, while previously cryptic, thrombogenic subendothelial substances eg.collagen become exposed to flowing blood. Circulating platelets recognize sites of vascular disruption and undergo the process of adhesion to the site of injury. von willebrand factor mediates platelet adhesion, which is

present in the extracellular matrix of sub endothelial vessel wall. The receptor of von willebrand factor on the platelet surface is localized in membrane glyco-protein (Gp) Ib, part of the platelet membrane Gp Ib/IX-V complex. The progression of platelet adhesion is also assisted by direct binding to subendothelial collagen via specific collagen receptors in platelet membranes

Activation

Adherent platelets then become activated. The platelet activation process results from the combined actions of several agonists that bind to their respective membrane receptors on adherent platelets and transmit platelet activating intracellular signals. Activated platelets then undergo release reaction during which they secrete pre-packaged constituents of their cytoplasmic granules. The constituents released from dense granules are ADP, ATP serotonin. The constituents released from alpha granules are soluble adhesive proteins (fibrinogen, von willebrand factor, thrombospondin, fibronectin), growth factors (PDGF, TGF α, TGF β), procoagulants (platelet factor 4, Factor V). Simultaneously, activated platelets synthesize de novo and release the potent platelet activator and vasoconstrictor thromboxane A2 (TXA2).

Aggregation

The activated platelets release certain products, including secreted granule constituents and TXA_2 mediate aggregation. During platelet aggregation (platelet-platelet interaction), additional platelets are recruited from circulation to the site of vascular injury. Ultimately an occlusive thrombus is formed.

At lower shear levels (eg. In venous circulation), the molecular glue that mediates aggregation is fibrinogen, which can be derived either from plasma or from the alpha granule releasate of activated platelets. At higher shear level, (eg. In arteries) von willebrand factor can substitute for fibrinogen as the ligand of aggregation. Fibrinogen or von willebrand factor binds to the specific platelet membrane receptor that are located in the Gp IIb/IIIa integrin complex and mediates aggregation and finally the platelet plug is formed. The platelet plug is anchored and stabilized by the fibrin mesh that develops simultaneously as the product of the coagulation cascade.

PLATELET VOLUME & CARDIOVASULAR DISEASE

The platelets have a major role in the biological events immediately forerunning the acute coronary events. The changes in platelet structure has a significant role in begetting a thrombus . The thrombus enrooting on a coronary atherosclerotic plaque is the ultimate cause for all acute myocardial infarctions. In unstable angina also thrombus is the major triggering factor[11] .

Platelet activation therefore plays a significant role in all acute coronary events. As the initial step in the pathogenesis of acute myocardial infarction is plaque erosion or rupture followed by platelet adhesion, activation and aggregation followed by thrombus formation, platelets with more activity will predispose to the occurrence of myocardial infarction.

Martin JF et al.in 1983 showed that mean platelet volume which represents platelet size relate mutually to their reactivity .

Jakubowski JA, Giles et al in 1992 described circulating platelets as having multifarious size, density, and reactivity. Their study showed that mean platelet volume is positively associated with indicators of platelet activity including expression of glycoprotein Ib and glycoprotein IIb/IIIa receptors .

Endler G, Bath P et al in 2004 proved in their study ,that patients with myocardial infarction and unstable angina are characterized with higher values of mean platelet volume as compared to those with stable angina or noncardiac chest pain, and recognized mean platelet volume as an independent risk factor for myocardial infarction and stroke .

Keskin O and Ulusoy RE et al in 2004 showed a poor clinical outcome among survivors of myocardial infarction associated with elevated MPV.

Corash ey al in 2000 in their study using in vitro aggregometry proved that large platelets are metabolically and enzymatically more active[25] than small platelets, and their thrombotic potential is much higher than the smaller ones which was explained by Karpatkin et al in 1972.

Mathur et al and Pathansali et al in 2001 showed that large platelets expressed higher levels of procoagulatory surface proteins such as P-selectin and glycoprotein IIIa .

Janusz Kochman,et al in 2005 studied the significance of Mean platelet Volume on admission and disclosed that it predicts impaired reperfusion and long term mortality in acute myocardial infarction treated with primary percutaneous coronary intervention

Large platelets are denser and aggregate more rapidly than their smaller counterparts and expressed more receptors per unit area (Pizuli et al 2000)

When Cox DA, Stone GW et al 2006 compared MPV for both STEMI and NSTEMI groups, they found higher MPV values for STEMI compared to healthy controls, which was consistent with larger and reactive platelets inciting an increased prothrombotic state leading to consumption of larger and reactive platelets

Platelet volume and prognosis following acute myocardial infarction

Hendra et al(1988) observed that all patients with severe cardiac failure had larger platelet volumes than patients with mild or no failure. Osuna et al (1998) stated that increase in mean platelet volume on admission was an independent risk factor for cardiac failure.

Increased MPV was found to be an independent risk factor for recurrent myocardial infarction by Martin et al (1982).

Yilmaz et al (2004) observed that in patients with dilated cardiomyopathy and in sinus rhythm, an increased MPV was associated with an increased incidence of left ventricular thrombus.

In contrast to the above observations, Cameron et al (1983) noted that the increase in MPV did not appear to provide any prognostic information after myocardial infarction. The value in patients who dies was no different from that of the survivors. The MPV did not correlate with the more established factors determining prognosis after myocardial infarction such as size of the infarct.

AGE, SEX AND MPV

Funiak et al (1994) observed increased MPV in patients of advanced age. In contrast Bancroft et al (2000) observed decreased MPV with advanced age. He

observed no difference between genders.

MPV AND SMOKING

Smokers were found to have an increased MPV (Tschope et al, 1989; Kario et al, 1992).

MPV AND OTHER DISEASES

An increase in MPV was observed in diabetics compared with non diabetics by Sharpe et al (1993).

Although Osuna et al (1998) observed a higher MPV in those with systemic hypertension, Bath et al (1996) observed no such effect.

Ford et al (1998) observed that patients with hyperthyroidism had increased MPV.

Bansal et al (2002) stated that MPV was increased in patients with chronic obstructive pulmonary disease and this could possibly contribute to an increased incidence of pulmonary embolism in these patients.

In chronic liver disease, MPV and platelet count are decreased (Jorgensen et al, 1984).

AIMS AND OBJECTIVES

AIMS AND OBJECTIVES

1) To investigate the association between mean platelet volume and acute coronary syndrome in patients with diagnosis of acute coronary disease, in comparison with control group

2) To find out the role of mean platelet volume in short term outcome after myocardial infarction

3) To identify whether any association exists between mean platelet volume and other selected factors like age ,sex, smoking, systemic hypertension and diabetes mellitus

4) To check the sensitivity and specificity of mean platelet volume when compared to Troponin-T

MATERIALS AND METHODS

MATERIALS AND METHODS

Setting : Department of Internal Medicine and Intensive coronary care unit , Thanjavur medical college, Thanjavur

Collaborative department: Department of cardiology, Thanjavur medical college ,Thanjavur

Design of study : Comparative cross sectional study

Period of study : April 2012 to November 2012

Sample size : Total 111, study group 86, control 25

Inclusion criteria : Patients who had history suggestive of acute coronary syndrome, whose ECG showed typical ST segment deviation with other laboratory evidence

Exclusion criteria :

1) Not having typical ECG changes
2) Presence of septicemia
3) Known cases of any haematological disorders
4) Presence of blood loss

5)Presence of hyperthyroidism

6) Presence of chronic heart disease

7) Presence of chronic renal failure

8) Past history of cerebrovascular accident

9) Known case of any malignancy

10) Past history of coronary artery disease

CONTROLS

Age and sex matched subjects who had atypical chestpain, without ECG or laboratory evidence of coronary artery disease or history of previous coronary artery disease were kept as controls

CONSENT

Informed consent was obtained from all those who participated in the study or their relatives

MATERIALS

Thus a total of 45 MI patients & 41 Unstable angina patients who satisfied the inclusion and exclusion criteria stated above were taken up for subsequent study. 25 age and sex matched subjects were kept as control.

DEFINITIONS USED FOR THE STUDY

1) Acute myocardial infarction (AMI) :

The diagnosis of AMI was established by three criteria accepted by WHO:

1. Ischaemic type of chest pain typical of AMI
2. Changes in serial ECG tracings typical of AMI
3. positive cardiac biomarkers

2) Unstable angina:

The diagnosis of unstable angina pectoris was established by the presence of unstable chest pain and typical ECG findings in the absence of elevated cardiac bio markers

3) smoking:

A subject was considered to be a smoker if he or she gives history of smoking within the past 20 years , persons who had quit smoking completely before 20 years were not considered as smokers

4) Systemic hypertension:

A subject was considered to have systemic hypertension if he or she was already diagnosed to have systemic hypertension and was on anti- hypertensive medications or if the systolic blood pressure during the

hospital stay was to be more than or equal to 140 mm hg and for diastolic B.P was more than or equal to 90 mm hg

5) Diabetes mellitus:

A subject was considered to have diabetes if he/she was already diagnosed to have diabetes mellitus or during the hospital stay, was found to have a

- fasting plasma glucose ≥ 126 mg/dl

-2 hr post prandial plasma glucose ≥ 200mg /dl

- symtoms of diabetes mellitus plus random blood sugar ≥200mg/dl

6) Left ventricular dysfunction:

Left ventricular dysfunction was divided to mild, moderate and severe according to ejection fraction on ECHO < 29% severe , 30-39% moderate , 40 -49% per mild

SHORT TERM OUTCOME

Outcome at the end of 7 days after MI was considered with respect to left ventricular dysfunction , occurrence of arrhythmia , occurrence of death.

METHODS

Selected socio-demographic , clinical and laboratory value was collected from patients and controls and recorded in proforma (enclosed in annexure)

1) Socio demographic data composed of

.age

.sex

. smoking

.diabetes and hypertension

2)clinical data

3)laboratory data

.Random blood sugar

.Total cholesterol

.ECG

.echocardiogram, troponin T

.platelet count

.mean platelet volume

ECG - 12 lead multi channel ECG was taken in all patients

ECHO-

Trans thoracic echo was done using NOS TRIVITROX in all the cases .

2- D ECHO, M- MODE ECHO was done to analysis the regional wall motion abnormality presence of clot & also to assess the left ventricular function. Colour Doppler was done to evaluate the presence of valvular regurgitation and also to assess the diastolic dysfunction.

For the above mentioned haematological parameters , 2ml of blood was withdrawn by vene puncture from the patient within 24 hrs of admission to the hospital. The puncture site was properly cleansed and blood withdrawn and collected in EDTA containing disposable tubes .The sample was transfused immediately to a quality controlled centre where the sample was analyzed for platelet volume. The instrument used for analysis was LOBAS MICROS OT 18 automated hematological analyzer made by ROCHE.

The instrument was started . After start up , a pipette appeared from the instrument . blood sample was fed to the instrument by the principal worker. The principle drew the necessary amount of blood and withdrew on its

own after taking the necessary amount of blood. A waiting time of 180 seconds appeared on the instrument, then at the end of 180 seconds a printout with the platelet count and mean platelet volume was ejected from the printer connected to the instrument.

The instrument was repeatedly standardized for quality control.

CONFLICT OF INTEREST

There was no conflict of interest

FINANCIAL SUPPORT

Nil

STATISTICAL ANALYSIS:

Data were entered in Microsoft excel spread sheet and analyzed utilizing the software STATA version 12 and SPSS version 17. ROC curve was calculated using MEDCALC.

OBSERVATIONS AND RESULTS

OBSERVATIONS AND RESULTS

Total number of subjects included in the study was 111. Among the 111 subjects 45 had myocardial infarction (MI), 41 unstable angina and 25 controls . Their baseline characters are provided below.

Age and Sex distribution

Age:

The age of MI cases ranged from 28 to 78 years with mean age 55.18±12.881, unstable angina ranged from 30 to 80 years with mean age 53.73±13.504 and control ranged from 32 to 68 years with mean age 49.20±10.516 . The distribution of cases and controls with respect to age is given in Table -1 given below:

Table – 1 (Age Distribution in the 3 Groups)

	N	Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean	
					Lower Bound	Upper Bound
MI	45	55.18	12.881	1.920	51.31	59.05
Unstable Angina	41	53.73	13.504	2.109	49.47	57.99
Control	25	49.20	10.516	2.103	44.86	53.54
Total	111	53.30	12.733	1.209	50.90	55.69

N- number, Std- standard.

One way ANOVA test was done and the ‘p’ value was 0.164 which proved that there was no significant difference in the distribution of age , between the groups

Sex composition :

Among the 86 cases studied in MI and Unstable angina groups, there were 33 malesand 12 females in MI group, 29 males and 12 females in the Unstable angina group. Among the control group, there were 15 males and 10 females. The sex composition is given below in Table – 2.

Table – 2 (Sex Composition in the Study groups)

		Cases		Control
		MI	Unstable angina	
SEX	Male	33	29	15
	Female	12	12	10

Chi- square test was done and the ‘p’ value was found to be 0.126(>.05). Thus there was no significant difference in the sex distribution among the groups

Comparison of Platelet Volume in Study Groups

The Mean Platelet Volume in MI group is 9.84±0.67 and the values ranged from 8.6 to 11, in Unstable angina group mean MPV is 9.07±0.77 and the values ranged from 7.0 to 10.6 and in the Control group mean platelet

volume is 6.85±0.73 and the values ranged from 6.0 to 8.4. The mean platelet volume values of the 3 groups is given below in Table – 3 .

Table – 3 (Mean Platelet Volume values in the 3 Study Groups)

	N	Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean	
					Lower Bound	Upper Bound
MI	45	9.842222	.6767197	.1008794	9.638913	10.045531
Unstable angina	41	9.078049	.7734702	.1207957	8.833911	9.322186
Control	25	6.852000	.7377443	.1475489	6.547474	7.156526
Total	111	8.886486	1.3592435	.1290137	8.630812	9.142161

One way ANOVA was done to compare the mean MPV in the 3 groups and the 'p' value was found to be significant. Hence the Mean MPV in the 3 groups were significantly different. The Results of One way ANOVA are given in Table – 4

Table-4

	Sum of Squares	Df	Mean Square	Sig.('p')
Between Groups	146.087	2	73.044	.000
Within Groups	57.142	108	.529	
Total	203.230	110		

Following ANOVA , Post Hoc Tests with Tukey and Bonferroni Methods were used to detect the Significance when each group was compared to the rest. Following this, the results showed that every group is significantly different individually from the rest. The Post Hoc tests results in Tukey method are given below in Table – 5 and for Bonferroni method in Table – 6 .

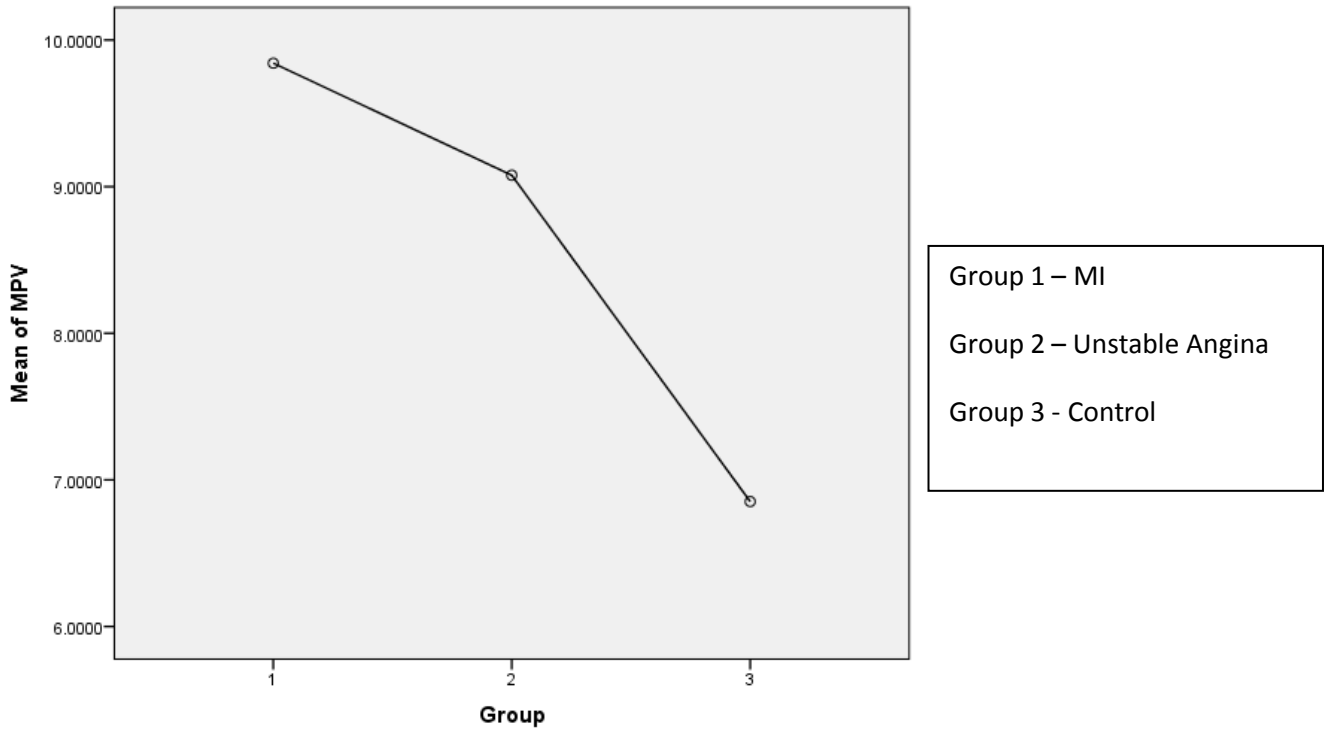
Table – 5 (Post Hoc Tests – Tukey Method)

	(I) Group	(J) Group	Mean Difference (I-J)	Std. Error	Sig.('p')
Tukey HSD	MI	Unstable Angina	.7641734*	.1570430	.000
		Control	2.9902222*	.1814430	.000
	Unstable Angina	MI	-.7641734*	.1570430	.000
		Control	2.2260488*	.1845770	.000
	Control	MI	-2.9902222*	.1814430	.000
		Unstable Angina	-2.2260488*	.1845770	.000

Table – 6 (Post Hoc Tests – Bonferroni Method)

	(I) Group	(J) Group	Mean Difference (I-J)	Std. Error	Sig.('p')
Bonferroni	MI	Unstable Angina	.7641734*	.1570430	.000
		Control	2.9902222*	.1814430	.000
	Unstable Angina	MI	-.7641734*	.1570430	.000
		Control	2.2260488*	.1845770	.000
	Control	MI	-2.9902222*	.1814430	.000
		Unstable Angina	-2.2260488*	.1845770	.000

Figure – 1 Plot of the Mean MPV in the 3 Groups



Comparison ofPlatelet counts in the Study Groups:

The platelet counts in the study groups were compared. In the MI group the mean platelet count was 141800±63350 and the values ranged from 75000 to 310000, in the Unstable angina group the mean was 138243±61436 and the values ranged from 80000 to 340000 and finally in the Control group the mean was 230800±56856 and the values ranged from 120000 to 340000. The mean and the standard deviation of the platelet count in the 3 groups in given below in Table – 7 .

Table – 7 (Mean Platelet count in the 3 groups)

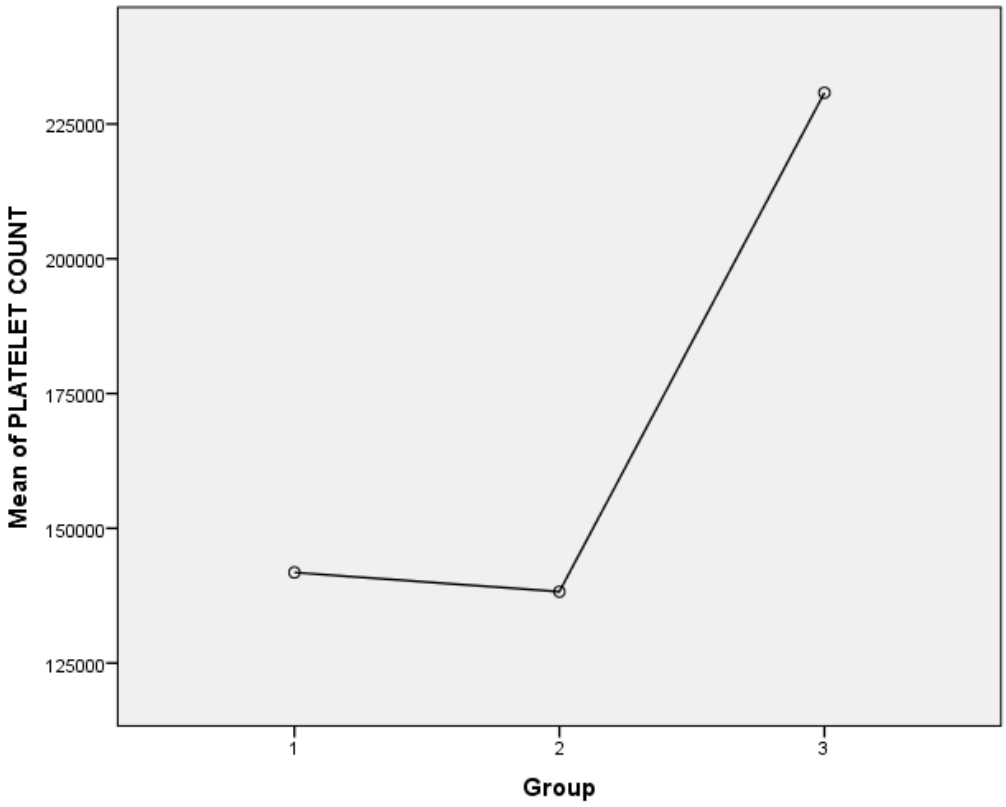
	N	Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean	
					Lower Bound	Upper Bound
1	45	141800.00	63350.970	9443.805	122767.26	160832.74
2	41	138243.90	61436.463	9594.764	118852.16	157635.64
3	25	230800.00	56856.545	11371.309	207330.77	254269.23
Total	111	160531.53	71652.294	6800.935	147053.68	174009.39

One way ANOVA was done and the mean platelet counts significantly differed in the 3 groups with a significant ‘p’ value . The results of the analysis are shown in Table – 8 .

Table- 8

	Sum of Squares	df	Mean Square	Sig.('p')
Between Groups	159596878664.030	2	79798439332.015	.000
Within Groups	405148760975.610	108	3751377416.441	
Total	564745639639.640	110		

Figure – 2 (Plot of the Mean Platelet Count in the 3 Groups)



Group 1 – MI

Group 2 – Unstable angina

Group 3 – Control

ROC Analysis (Receiver operating characteristic)

This analysis is used to compare mean platelet volume with a Standard diagnostic test like Troponin T as in this study in order to assess the Sensitivity and Specificity of Mean platelet Volume in detecting MI.

ROC curve

Diagnostic Test	MPV
Standard Diagnostic Test	Troponin T Test Strip.

Sample size	111
Positive group :	45
Negative group :	66

On performing the analysis in Medcalc statistical software , a curve was obtained with the following features :

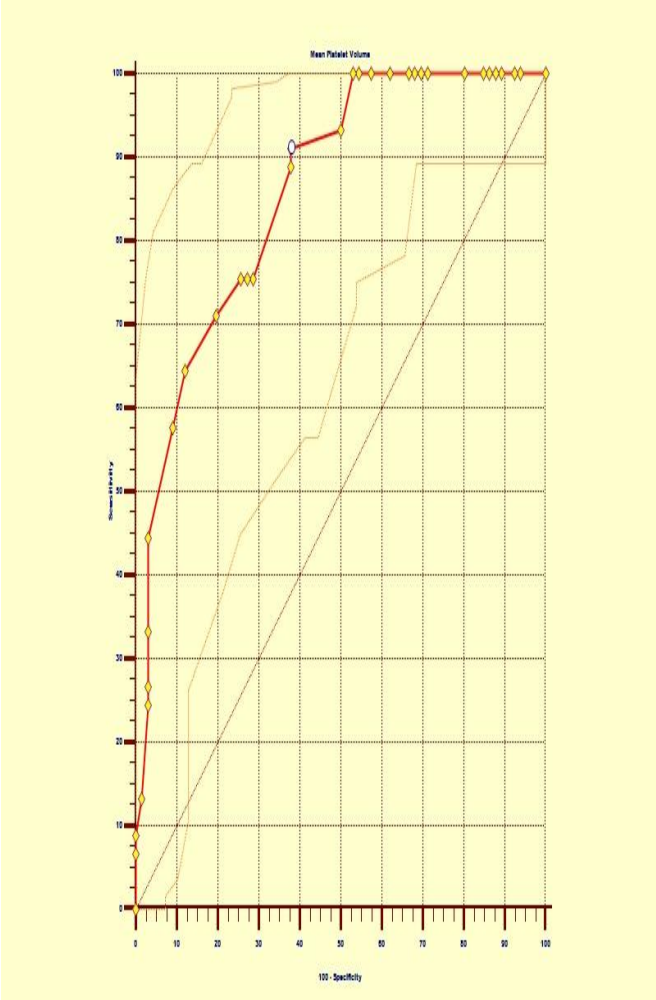
Area under the ROC curve (AUC)	0.858
Standard Error[a]	0.0342
95% Confidence interval[b]	0.779 to 0.917
z statistic	10.477
Significance level P (Area=0.5)	<0.0001

Then various cut off points of MPV were chosen and their sensitivity and specificity were checked in the Curve

Cut off value of MPV	Sensitivity	95% CI	Specificity	95% CI
>=6	100.00	92.1 - 100.0	0.00	0.0 - 5.4
>6	100.00	92.1 - 100.0	6.06	1.7 - 14.8
>6.1	100.00	92.1 - 100.0	7.58	2.5 - 16.8
>6.2	100.00	92.1 - 100.0	10.61	4.4 - 20.6
>6.3	100.00	92.1 - 100.0	12.12	5.4 - 22.5
>6.4	100.00	92.1 - 100.0	13.64	6.4 - 24.3
>6.5	100.00	92.1 - 100.0	15.15	7.5 - 26.1
>6.6	100.00	92.1 - 100.0	19.70	10.9 - 31.3
>7	100.00	92.1 - 100.0	28.79	18.3 - 41.3
>7.2	100.00	92.1 - 100.0	30.30	19.6 - 42.9
>7.3	100.00	92.1 - 100.0	31.82	20.9 - 44.4
>7.4	100.00	92.1 - 100.0	33.33	22.2 - 46.0
>7.8	100.00	92.1 - 100.0	37.88	26.2 - 50.7
>8	100.00	92.1 - 100.0	42.42	30.3 - 55.2
>8.1	100.00	92.1 - 100.0	45.45	33.1 - 58.2
>8.4	100.00	92.1 - 100.0	46.97	34.6 - 59.7
>8.6	93.33	81.7 - 98.6	50.00	37.4 - 62.6
>8.8 *	91.11	78.8 - 97.5	62.12	49.3 - 73.8
>8.9	88.89	75.9 -96.3	62.12	49.3 -73.8
>9	75.56	60.5 - 87.1	71.21	58.7 - 81.7

Cut off value of MPV	Sensitivity	95% CI	Specificity	95% CI
>9.1	75.56	60.5 - 87.1	72.73	60.4 - 83.0
>9.2	75.56	60.5 - 87.1	74.24	62.0 - 84.2
>9.4	71.11	55.7 - 83.6	80.30	68.7 - 89.1
>9.6	64.44	48.8 - 78.1	87.88	77.5 - 94.6
>9.8	57.78	42.2 - 72.3	90.91	81.3 - 96.6
>10	44.44	29.6 - 60.0	96.97	89.5 - 99.6
>10.1	33.33	20.0 - 49.0	96.97	89.5 - 99.6
>10.2	26.67	14.6 - 41.9	96.97	89.5 - 99.6
>10.3	24.44	12.9 - 39.5	96.97	89.5 - 99.6
>10.4	13.33	5.1 - 26.8	98.48	91.8 - 100.0
>10.6	8.89	2.5 - 21.2	100.00	94.6 - 100.0
>10.8	6.67	1.4 - 18.3	100.00	94.6 - 100.0
>11	0.00	0.0 - 7.9	100.00	94.6 - 100.0

In ROC curve analysis sensitivity is taken along the Y axis and 100-specificity is taken along the X axis. Curve is plotted as per the values of MPV compared to Trop- T which was the major diagnostic test. On plotting the curve , the top left portion of the curve is chosen to get the cut-off point with maximum sensitivity and specificity.So in my study the cut –off value of 8.8fl was at the top left point and it satisfied the criteria with the highest Youden Index. It has 91.11% sensitivity and 62.12% specificity



ROC CURVE

Possible determinants of MPV as analysed by Multiple Linear Regression

Mean Platelet Volume as a quantitative dependent variable was analysed with independent variables like age, Blood sugar and Blood Cholesterol values through Multiple linear regression. The Regression Co-efficients of the Independent variables are given below in Table – 8 .

Table – 8 (Regression Coefficients of the Independent Variables)

Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.('p')
		B	Std. Error	Beta		
1	(Constant)	3.151	1.130		2.789	.006
	CHOLESTEROL	.020	.005	.355	3.972	.000
	SUGAR	.006	.003	.183	2.062	.042
	AGE	.021	.009	.193	2.194	.030

The study showed that an increase in age, total cholesterol or random blood sugar by one unit will increase the MPV by 0.193, 0.183 and 0.355 respectively as evidenced by the beta coefficients

RELATIONSHIP BETWEEN MPV AND OTHER PARAMETERS

The mean platelet volume is compared with several parameters.

Age group comparisons

The Mean platelet volume was found in different age groups and it was analysed with One way ANOVA to find any significant difference . The 'p' value was found to be 0.114 and hence there was no significant

difference on comparing the mean platelet volume in all the age groups. Table – 9 summarises the mean and the standard deviation of the Mean platelet volume in the different age group . Table – 10 shows the results of the One way ANOVA done to compare the different age groups and their mean platelet volume.

Table – 9 (Relationship between Age & MPV)

Age Group	N	Mean	Std. Deviation	95% Confidence Interval for Mean	
				Lower Bound	Upper Bound
< 30	1	10.100000	.	.	.
30 – 39	15	8.573333	1.3040961	7.851149	9.295518
40 – 49	25	8.836000	1.4174155	8.250920	9.421080
50 – 59	26	8.507692	1.6716275	7.832507	9.182877
60 – 69	34	9.041176	1.1279151	8.647628	9.434725
70 – 79	10	9.820000	.5865151	9.400432	10.239568
Total	111	8.886486	1.3592435	8.630812	9.142161

Table – 10 (One way ANOVA results on age groups with MPV)

	Sum of Squares	df	Mean Square	F	Sig. ('p')
Between Groups	16.266	5	3.253	1.827	0.114
Within Groups	186.964	105	1.781		
Total	203.230	110			

Group 2 = 30 – 39 years

Group 3 = 40 – 49 years

Group 4 = 50 – 59 years

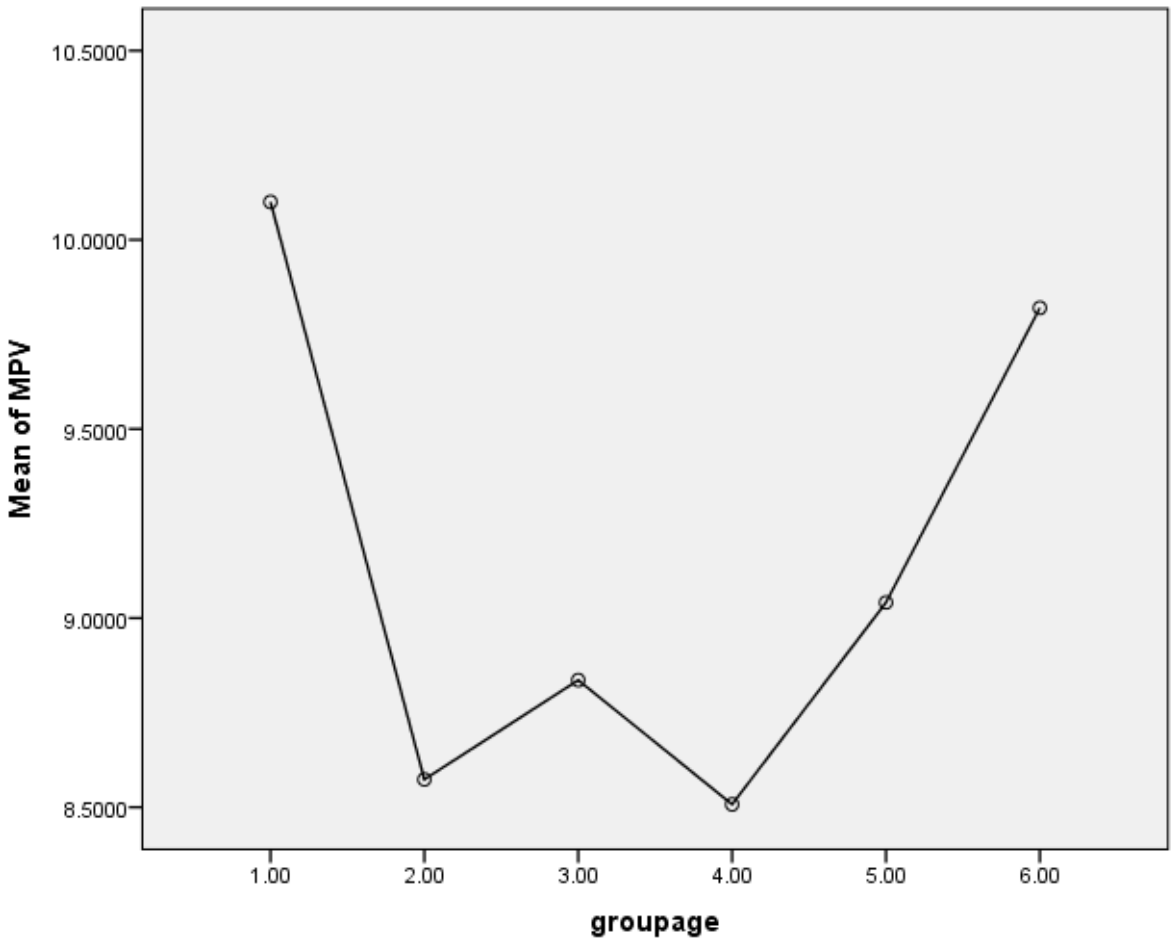
Group 5 = 60 – 69 years

Group 6 = > 70 years

df- degrees of freedom

The 'p' value was not found to be less than .05, showing no statistically significant difference between the age groups. The highest MPV was found in the age group between 70-79 years.

Figure – 3 (Mean plot of the MPV in the different age groups)



Relationship between Sex and MPV

The MPV for males was 9.01±1.30and the MPV for females was 8.59±1.45. On analysing the MPV with the two sex by Independent 't' test , the 'p' value was not significant. Hence the MPV is not significantly different between the 2 sexes. Table – 11 shows the MPV in the 2 sex and the Table – 12 shows the result of the Independent 't' test.

Table – 11 (MPV in the sex groups)

	SEX	N	Mean	Std. Deviation	Std. Error Mean
MPV	Males	77	9.014286	1.3059292	.1488244
	Females	34	8.597059	1.4513286	.2489008

Table – 12 (Independent 't' test results of sex groups with MPV)

		Levene's Test for Equality of Variances		t-test for Equality of Means	
		F	Sig.	t	Df
MPV	Equal variances assumed	.983	.324	1.499	109
	Equal variances not assumed			1.439	57.616

Relationship between smoking and MPV

The Mean platelet count was compared between Smokers and Non smokers. The number of smokers in MI , Unstable angina and Control groups were 22, 10 and 3 respectively. The number of non-smokers in MI, Unstable angina and Control groups were 23, 31 and 22 respectively.

Table – 13 shows the distribution of smokers and non-smokers in the 3 groups.

Table – 13 (Smokers and Non- smokers in the 3 groups)

		Group		
		MI	Unstable Angina	Control
SMOKING	Yes	22	10	3
	No	23	31	22

The mean platelet volume was compared between the smokers and non smokers by independent 't' test and the 'p' value was found to be not significant. The MPV among smokers was 9.41±1.19 and among non-smokers it was 8.64±1.36. Table – 14 shows the MPV among smokers and non-smokers. Table – 15 shows the result of the Independent 't' test to compare the MPV between smokers and non-smokers.

Table – 14 (MPV among smokers and non-smokers)

	SMOKING	N	Mean	Std. Deviation	Std. Error Mean
MPV	Yes	35	9.414286	1.1936456	.2017629
	No	76	8.643421	1.3689252	.1570265

Table – 15 (Results of Independent 't' test comparing smoking groups with MPV)

		Levene's Test for Equality of Variances		t-test for Equality of Means	
		F	Sig.	t	Df
MPV	Equal variances assumed	2.162	.144	2.866	109
	Equal variances not assumed			3.015	75.161

Relationship between systemic hypertension & MPV

The number of hypertensives in MI, Unstable angina and Control groups were 28, 20 and 3 respectively. The number of non-hypertensives in MI, Unstable angina and Control groups were 17, 21 and 22 respectively. Table – 16 shows the distribution of hypertensives and non – hypertensives in all the 3 study groups.

Table – 16 (Distribution of Hypertensives and Non-hypertensives)

		Group		
		MI	Unstable Angina	Control
Hypertension	Yes	28	20	3
	No	17	21	22

The MPV among hypertensives was 9.42±1.03 and among non-hypertensives was 8.43±1.44. The MPV was compared among hypertensives and non-hypertensives by independent 't' test and the 'p' value turned out to be significant. Table – 17 shows the MPV among hypertensives and non-hypertensives. Table – 18 shows the results of the Independent 't' test comparing MPV between hypertensives and non hypertensives.

Table – 17 (MPV among hypertensives and non-hypertensives)

	Hypertension	N	Mean	Std. Deviation	Std. Error Mean
MPV	Yes	51	9.421569	1.0309828	.1443665
	No	60	8.431667	1.4442747	.1864551

Table – 18 (Independent 't' test results comparing MPV among hypertensives and non-hypertensives)

		Levene's Test for Equality of Variances		t-test for Equality of Means	
		F	Sig.('p')	T	Df
MPV	Equal variances assumed	14.078	.000	4.088	109
	Equal variances not assumed			4.198	105.994

Relationship between Diabetes Mellitus & MPV

The number of diabetics in MI, Unstable angina and the Control groups was 17, 10 and 6 respectively. The number of non-diabetics among MI, Unstable angina and control groups was 28, 31 and 19 respectively. Table – 19 shows the distribution of diabetics and non diabetics in the 3 groups.

Table – 19 (Distribution of Diabetics and non diabetics)

		Group		
		MI	Unstable angina	Control
DIABETES	Yes	17	10	6
	No	28	31	19

The MPV among diabetics was 9.25±1.29 and among non-diabetics was 8.73±1.36. The MPV was compared between diabetics and non diabetics using Independent 't' test and the 'p' value turned out to be not significant. Table – 20 shows the MPV among diabetics and non diabetics. Table 21 – shows the results of the independent 't' test done to compare MPV between diabetics and non-diabetics.

Table – 20 (MPV among Diabetics and Non-Diabetics)

	DIABETES	N	Mean	Std. Deviation	Std. Error Mean
MPV	Yes	33	9.254545	1.2968931	.2257601
	No	78	8.730769	1.3629902	.1543282

Table – 21 (Independent 't' test results comparing MPV between Diabetics and Non Diabetics)

		Levene's Test for Equality of Variances		t-test for Equality of Means	
		F	Sig.('p')	t	Df
MPV	Equal variances assumed	.062	.804	1.877	109
	Equal variances not assumed			1.915	63.163

Relationship between ejection fraction & MPV

The Ejection fraction was divided into 4 groups ≤29, 30 – 39 , 40 – 49 and ≥50. The MPV in these groups was 10.7±0.25, 10.04±0.55, 9.83±0.61 and 9.44±0.67 respectively. Table – 22 shows the MPV in all the different groups.

Table – 22 (Mean Platelet Volume among different Ejection Fraction Groups)

	N	Mean Platelet Volume	Std. Deviation	Std. Error
≤29	4	10.700000	.2581989	.1290994
30 - 39	9	10.044444	.5525195	.1841732
40 - 49	19	9.836842	.6130167	.1406357
≥50	13	9.446154	.6703424	.1859195
Total	45	9.842222	.6767197	.1008794

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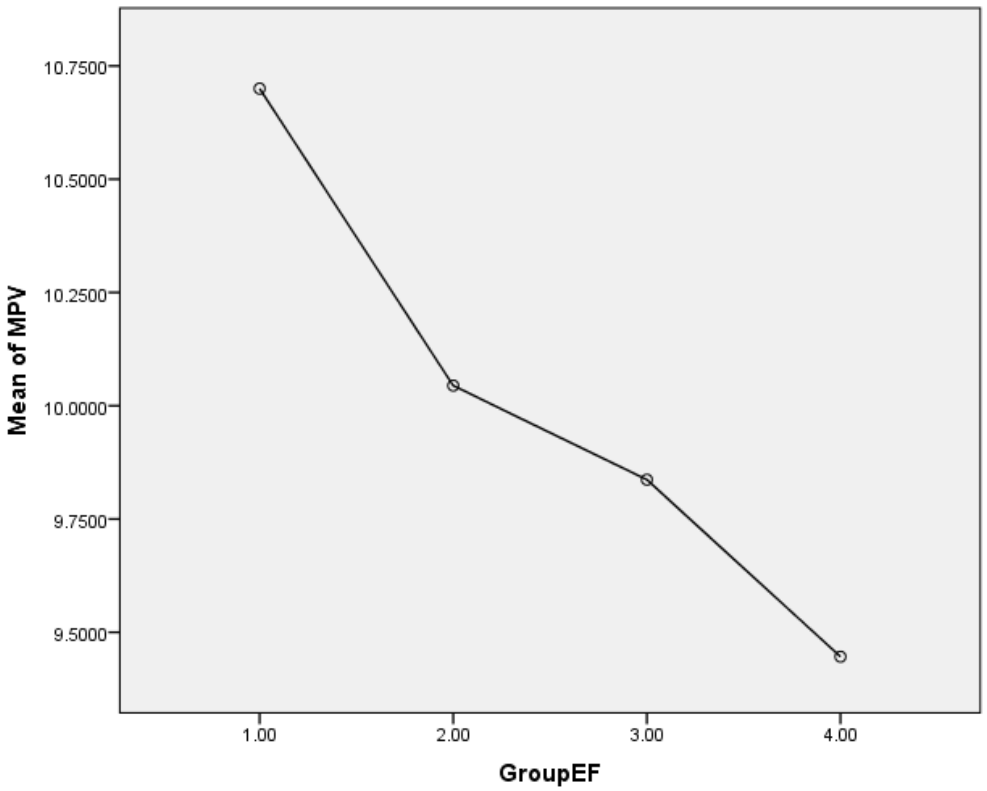
The mean platelet volume was compared in the 4 different groups by One way ANOVA and the 'p' value turned out to be significant. Hence the mean platelet volume is significantly different in each of these groups and then on

seeing the mean platelet volumes in the different groups , it's clear that in patients with Ejection Fraction ≤29 , the mean platelet volume is the highest. Hence we can conclude mean platelet volume is significantly different and higher as the ejection fraction reduces. The Following Table – 23 shows the results of One way ANOVA done to compare the MPV among the different ejection fraction groups.

Table – 23 (Results of One Way ANOVA after comparing the MPV in all the different Ejection Fraction groups)

	Sum of Squares	Df	Mean Square	F	Sig.('p')
Between Groups	5.351	3	1.784	4.942	.005
Within Groups	14.799	41	.361		
Total	20.150	44			

Figure – 4 (Mean Platelet Volume Plots among the different Ejection Fraction Groups)



Group EF 1 = ≤29

Group EF 2 = 30 – 39

Group EF 3 = 40 – 49

Group EF 4 = ≥50

Relationship between arrhythmias and MPV

The mean platelet volume among patients with arrhythmia was 9.83±0.44 and among patients without arrhythmia was 9.84±0.72. The mean platelet volume was compared in these 2 groups of patients by Independent 't' test and 'p' value was found to be insignificant. Table – 24 shows the Mean Platelet Volume in the 2 groups of Patients with and without arrhythmia. Table 25 – shows the results of the Independent 't' test .

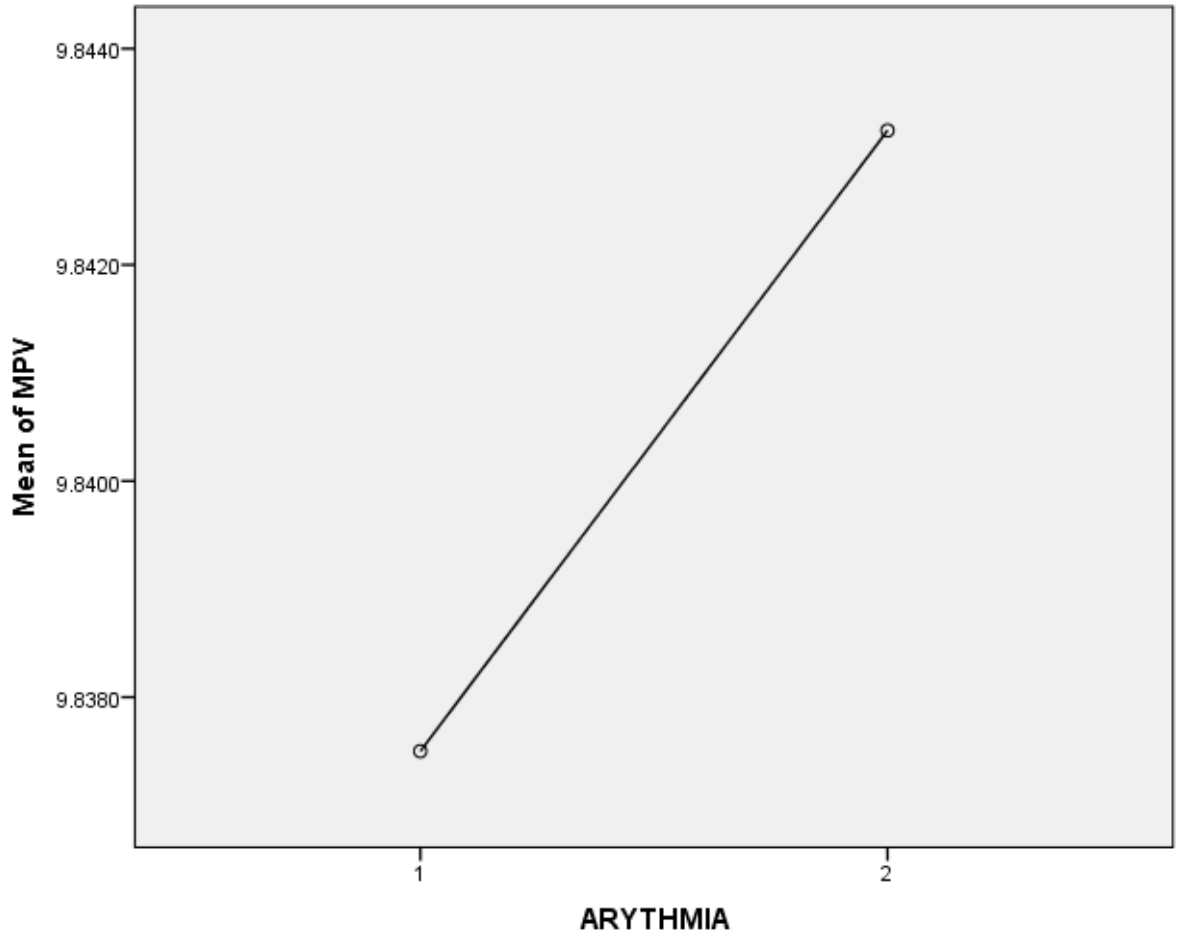
Table – 24 (Mean Platelet Volume among arrhythmics and Non arrhythmics)

	N	Mean	Std. Deviation	Std. Error
Arrhythmics	8	9.837500	.4405759	.1557671
Non-Arrhythmics	37	9.843243	.7224728	.1187738
Total	45	9.842222	.6767197	.1008794

Table – 25 (Results of Independent 't' test comparing MPV between Arrhythmics and Non arrhythmics)

	Sum of Squares	Df	Mean Square	F	Sig.('p')
Between Groups	.000	1	.000	.000	0.983
Within Groups	20.150	43	.469		
Total	20.150	44			

Figure – 5 (MPV among Arrythmics and Non Arrhythmics)



1 – Arrhythmics

2 – Non Arrhythmics

Relationship between survival without complication and MPV

The MPV was compared among patients who survived without complications and those with complications. The mean was 9.62±0.71 and 10.09±0.54 respectively. The 2 group of patients were compared with their

means by Independent ‘t’ test and the ‘p’ value came out to be significant. Hence the MPV in patients with Complications is significantly different and higher than the patients without complications. Table – 26 shows the MPV among the 2 groups of patients. Table – 27 shows the results of the Independent ‘t’ test with the significant ‘p’ value.

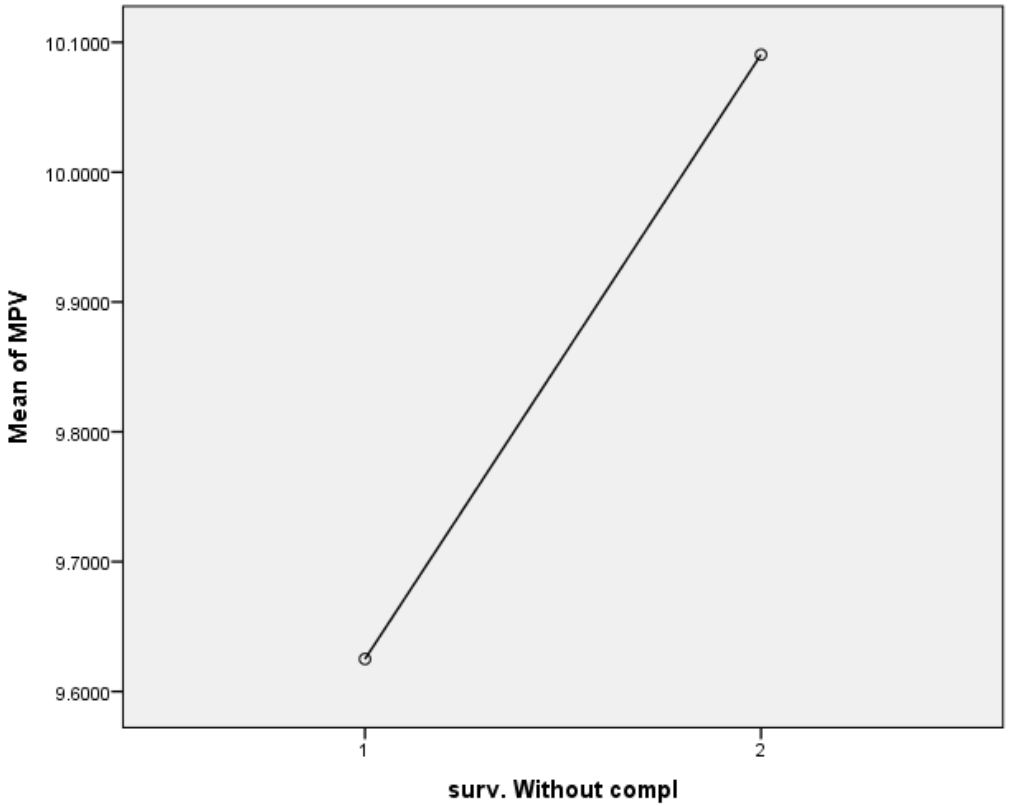
Table – 26 (MPV among patients who had complications and without complications)

	N	Mean	Std. Deviation	Std. Error
without Complications	24	9.625000	.7133814	.1456184
With Complications	21	10.090476	.5485479	.1197030
Total	45	9.842222	.6767197	.1008794

Table – 27 (Results of Independent ‘t’ test comparing the MPV in patients who survived without complications and with complications)

	Sum of Squares	df	Mean Square	F	Sig.(‘p’)
Between Groups	2.427	1	2.427	5.888	.020
Within Groups	17.723	43	.412		
Total	20.150	44			

Figure – 5 (Mean Platelet Volume Plots among patients without complications and with Complications)



1 – without Complications

2 – with Complications

Relationship between occurrence of death and MPV :

The mean platelet count was compared among patients who died and those who did not . The mean was 10.53±0.35 and 9.73±0.65 respectively in the 2 groups. The 2 groups were compared by Independent 't' test and the 'p' value turned to be significant. Hence the MPV in patients who died is significantly different and higher than the patients who did not die. Table – 28 shows the mean platelet volume among the patients those who died and those who did not

. Table – 29 shows the results of the Independent ‘t’ test and the ‘p’ value turned out to be significant . Hence the MPV among the patients who died is significantly different and higher than the patients who did not die

.

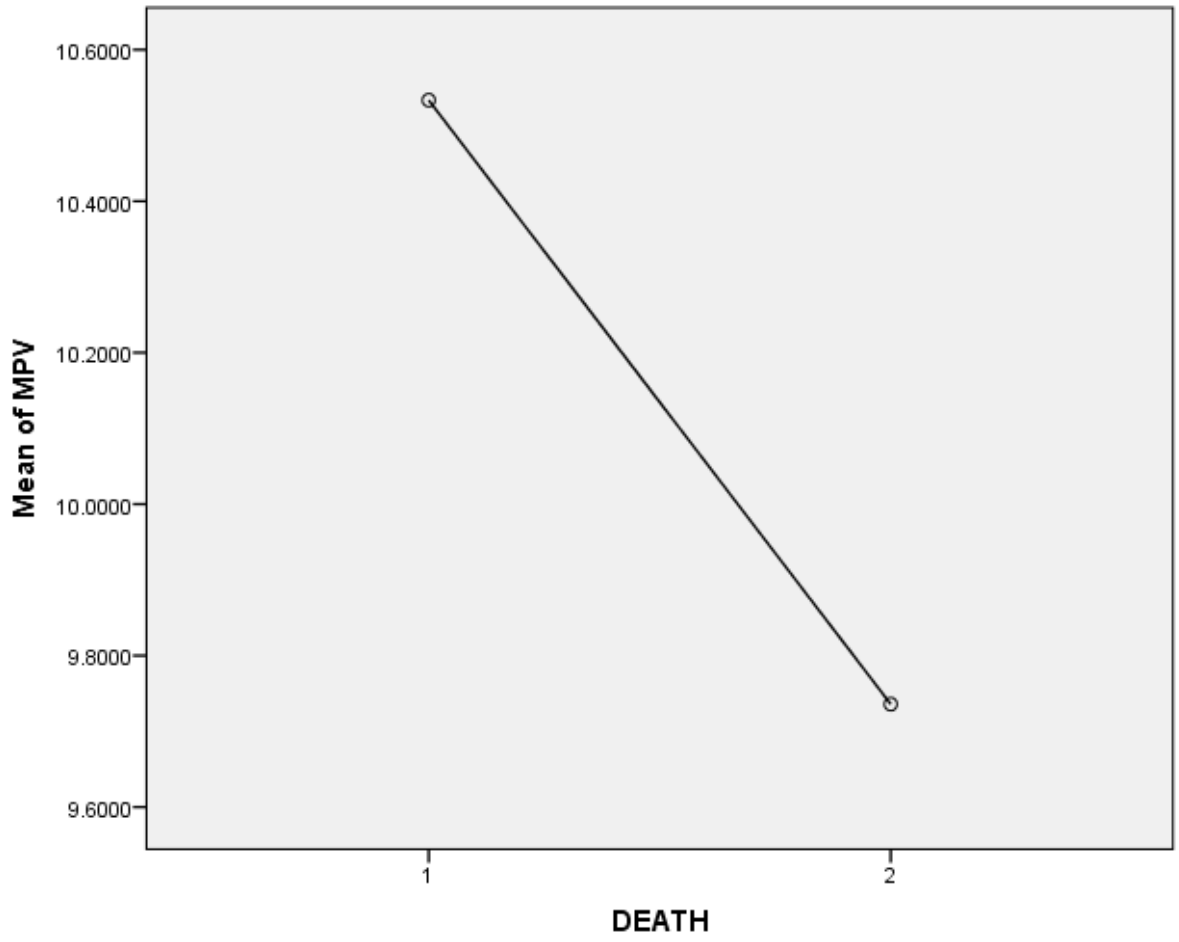
Table – 28 (Mean Platelet Volume among patients who died and who did not

	N	Mean	Std. Deviation	Std. Error
Patients who died	6	10.533333	.3502380	.1429841
Patients who didn’t die	39	9.735897	.6535277	.1046482
Total	45	9.842222	.6767197	.1008794

Table – 29 (Result of Independent ‘t’ test comparing MPV in patients who died and those who did’t)

	Sum of Squares	df	Mean Square	Sig.(‘p’)
Between Groups	3.307	1	3.307	.006
Within Groups	16.843	43	.392	
Total	20.150	44		

Figure – 6 (MPV among patients who died and those who didn't die)



1 – Patients who died

2 – Patients who did not die.

DISCUSSION

DISCUSSION

Coronary artery disease is a major cause of morbidity and mortality in industrialized countries and is becoming a major problem in developing countries like India. The risk of acute coronary syndrome is significantly increased by the endogenous and exogenous risk factors like diabetes, systemic hypertension, smoking and hypercholesterolemia. The individual risk for myocardial infarction is also increased by these factors. However they only explain a part of the cases and there may be other relevant risk factors which need to be identified. The thrombogenic phase is started by the rupture of an atherosclerotic plaque. The platelets play an important role for the progression of the thrombus[49].

The function and activation of platelets are directly indicated by its volume. The secretory granules and mitochondria in larger platelets are significantly higher and hence they are more active than smaller platelets .The larger platelets are hyperactive and leads to the formation and dissemination of intracoronary thrombus[12].This may again accelerate the evolution of clinical state called as acute coronary syndrome[12]. Van der Loo et al , in their study, claimed that platelet volume was an important biological

variable to determine platelet reactivity . They also suggested that elevated platelet volume measured after MI might be a determinant factor for future ischemic episodes and death. In this study an attempt was made to find out if any association existed between the platelet size and acute coronary syndrome among Indian population as reports are scanty.

In this study the age of MI cases ranged from 28 to 78 years with mean age 55.18±12.881, unstable angina ranged from 30 to 80 years with mean age 53.73±13.504. This corresponds to the pattern reported in India.

In the present study there was no significant difference in MPV between the age groups . Funiak et al (1994), in their study, found that MPV was significantly increased in platelets of advanced age and was statistically significant[16]. Bancroft et al (2000) stated that MPV decreases with age[46]. The present study did not show any difference in MPV between the age groups , but age was found to be a determinant factor for MPV on multiple linear regression analysis.

Among the 45 MI cases there were 33 males (73%) and 12 females(26%). Among the 41 unstable angina group, there were 29 males (70%) and 12(30%) females. Before menopause, women have a lower age adjusted incidence and mortality for coronary heart disease than men. This suggest a major role for estrogen in delaying progression of atherosclerosis. This effect results from beneficial action of estrogen on lipid fractions. Estrogen reduces LDL-C by 10-15% while increasing HDL-C

Ridwan Mercan et al , in 2010 did a comparison study on MPV between MI, Unstable angina and control groups. They found out that MPV was significantly higher in MI and Unstable angina groups when compared to normal groups. They claimed that MPV was higher in acute coronary syndrome.

In consistent with these findings, the present study also found out a high normal MPV in MI and Unstable angina when compared to control groups.

In the present study the Mean Platelet Volume in MI group is 9.84±0.67 and the values ranged from 8.6 to 11, in Unstable angina group mean MPV is 9.07±0.77 and the values ranged from 7.0 to 10.6 and in the Control group mean platelet volume is 6.85±0.73 and the values ranged from 6.0 to 8.4. The MPV was found to significantly different between these three groups. The mean MPV was higher in MI group when compared to other groups. It was found to be statistically significant. The mean MPV in Unstable angina group was higher when compared to control group, while lower when compared to MI group. The difference was found to be statistically significant.

Previous studies on MPV and acute coronary syndromes have given good correlations. Kishk et al. in their study, compared AMI patients to stable angina pectoris and control groups and detected that the former group had lower platelet count and higher MPV . They suggested, based on their study, that higher MPV and decreased platelet count may be a major risk factor for acute myocardial infarction[7]. In consistent with these findings, in present study

MPV was significantly higher and platelet count was lower in acute myocardial infarction group, compared to control groups

Puzzili et al. , in their study, found out that, unstable angina pectoris patients showed larger MPV, compared to stable angina and control groups [11]. In that study, they also detected that MPV was higher in unstable angina pectoris subjects who required emergent angioplasty, compared to the rest of unstable angina pectoris patients. With all these evidence they claimed that large volume platelets bestowed the formation of thrombus in coronary artery and led to reduction of platelet counts. In consistent with these findings, the present study showed that MPV was significantly higher and platelet count to be lower in unstable angina pectoris group than those in control groups.

Halbmayer et al (1995) stated that MPV did not differ significantly between MI patients and controls in their study. In contrast to this Cameron et al (1983) found an increased mean platelet volume among those with acute myocardial infarction compared to controls. Similar findings were observed by Martin et al(1983) in their study. Large platelets are denser, they produce more thromboxane A2 per unit volume of platelet cytoplasm. Larger platelets aggregate more rapidly upon collagen challenge, release more serotonin and other granule contents and express more receptors per unit area (Pizzuli et al). So an increased MPV , as an indicator of larger , more reactive platelets, may represent a risk factor for myocardial infarction(Endler et al).

The question arises whether the increase in platelet volume occurs before the acute coronary event or does it occur as a response to the platelet consumption in ACS. Martin et al , who did a study on MPV in acute myocardial infarction , measured mean platelet volume within 12 hrs of admission to hospital and then later at 6 weeks. They stated that mean platelet volume was increased before the occurrence of MI and depicted the following explanations. The increase in platelet volume seen within the first 12 hrs of admission suggested that the increase was present before infarction, as the life span of platelet is about 8 days. More than 90% of the platelet population whose distribution was measured after MI were circulating before the vascular occlusion occurred.

Further proof that the increase in MPV occurs before the myocardial infarction is got from the study conducted by Endler et al (2002). They evaluated mean platelet volume in patients presenting with acute myocardial infarction and in patients with history of previous myocardial infarction. They found out that MPV was significantly raised in those with acute MI. This further adds to the proof that raised MPV precedes the occurrence of MI.

O'Malley et al (1995) conducted a similar study of MPV estimation in stroke patients. They estimated MPV in stroke patients within 48 hrs of admission and also at 6 months later and compared it with controls. They found that MPV was significantly raised in stroke patients when compared to controls.

They suggested that the changes in MPV might have preceded the vascular event and is unlikely due to the platelet consumption at the infarct site. They said that since the average life span of platelets is about 8 days, the elevated MPV seen within the first 48 hrs after stroke represented platelets released before infarction. They also added that, the fact that the observed increase in MPV had remained unchanged in post stroke survivors was further evidence that changes in MPV were likely to have preceded the acute event.

The platelet counts in the study groups were compared. In the MI group the mean platelet count was 141800±63350 and the values ranged from 75000 to 310000, in the Unstable angina group the mean was 138243±61436 and the values ranged from 80000 to 340000 and finally in the Control group the mean was 230800±56856 and the values ranged from 120000 to 340000. The mean platelet count was found to be significantly different all the three groups. The MI and unstable angina group had significantly lower platelet count when compared to the control group. This finding was correlating to the study conducted by Cameroon et al (1983) , as they noticed that the patients with acute MI had a reduced platelet count when compared to the control groups. They observed a reduced platelet count and increased MPV in patients with MI. The observation in our study runs parallel to the findings of above workers.

In the present study MPV was independent of genders. The MPV for males was 9.01±1.30and the MPV for females was 8.59±1.45. The test

showed no statistical significant difference. This is in parallel with the observation made by Bancroft et al (2000).

The Mean platelet count was compared between Smokers and Non smokers. The number of smokers in MI , Unstable angina and Control groups were 22, 10 and 3 respectively. The number of non-smokers in MI, Unstable angina and Control groups were 23, 31 and 22 respectively .The Mean platelet volume was compared between the smokers and non smokers by independent 't' test and the 'p' value was found to be not significant. The MPV among smokers was 9.41±1.19 and among non-smokers it was 8.64±1.36. The study showed an increased prevalence of smoking habit among those with acute coronary syndrome. Although the mean MPV was higher among smokers compared to non smokers, the relationship was not statistically significant. Tschope et al(1989) and Kario et al(1985) in separate studies found smokers to have an increased MPV. Kishk et al (1985) observed no relation between smoking and MPV. Matsuo et al (1992) found out a significant increase in MPV among elderly smokers. They claimed that the increase in MPV due to smoking will also contribute to the formation of atherosclerotic plaque. However the present study did not show any statistical correlation. Larger sample size may be needed for establishing such correlations.

The relationship between MPV and systemic hypertension was studied. The number of hypertensives in MI, Unstable angina and Control groups were 28, 20 and 3 respectively. The number of non-

hypertensive in MI, Unstable angina and Control groups were 17, 21 and 22 respectively. The MPV among hypertensive was 9.42±1.03 and among non-hypertensive was 8.43±1.44. The MPV was compared among hypertensive and non-hypertensive by independent‘t’ test and the ‘p’ value turned out to be significant. Osuna et al (1998) also observed a higher MPV in those with systemic hypertension. Erkan coban et al (2005) in their study found out that MPV was significantly higher among patients with essential hypertension .Hyan ah chang et al (2010), in their study, found out that MPV is significantly raised in systemic hypertension. The present study, like the above mentioned works, showed similar correlation between systemic hypertension and MPV. Ntaios G et al (2011) studied the significance of MPV in stroke and even proved that systemic hypertension is an independent predictor of MPV .

The relationship between MPV and diabetes mellitus was studied. The number of diabetics in MI, Unstable angina and the Control groups was 17, 10 and 6 respectively. The number of non-diabetics among MI, Unstable angina and control groups was 28, 31 and 19 respectively. The MPV among diabetics was 9.25±1.29 and among non-diabetics was 8.73±1.36. The MPV was compared between diabetics and non diabetics using Independent‘t’ test and the ‘p’ value turned out to be not significant. On doing multiple linear regression analysis, random blood sugar was found to determine the MPV. This study showed that as the random blood sugar increases by 1, the MPV gets raised by 0.193. Sharpe et al (1993) showed that MPV was significantly increased in

diabetic subjects when compared to non-diabetics. They stated that since the platelet size is a determinant of platelet function, with larger platelets being more reactive per unit volume, platelets might play a part in the micro and macro vascular complications of diabetes mellitus. The fact that in our study, no relationship was observed, may be due to the small sample size.

ROC curve analysis was done in this study to compare the mean platelet volume with a standard diagnostic test like Trop-T and assess the Sensitivity and Specificity of Mean platelet Volume in detecting MI. The cut off value was found to be 8.8fl with a sensitivity of 91.11% and specificity of 62.12%. Guisseppe lippe et al (2009) , in their study found the cut off of MPV as 9.0 fl with negative and positive predictive value of 83% and 43% respectively. They suggested that as MPV is a simple and inexpensive laboratory measurement, it might be considered a useful rule-out test, along with other conventional cardiac biomarkers for the risk stratification of acute coronary syndrome patients admitted to the emergency departments.

Mean platelet volume and its relation to various outcome within 7 days after admission was studied to determine its prognostic significance. The various outcomes studied were ejection fraction, arrhythmias , cardiac failure and death. The Ejection fraction was divided into 4 groups ≤29, 30 – 39 , 40 – 49 and ≥50. The MPV in these groups was 10.7±0.25, 10.04±0.55, 9.83±0.61 and 9.44±0.67 respectively. The mean platelet volume

was significantly different and higher as the Ejection Fraction reduces. The highest MPV was obtained in ejection fraction ≤29. Hendra et al (1998) stated that all patients with severe cardiac failure had larger platelet volumes than patients with mild or no failure. Osuna et al(1998) also observed that an increased platelet volume was related to a higher risk of cardiac failure. The present study also showed a significant relation between MPV and ejection fraction.

The Mean Platelet Volume among patients with arrhythmia was 9.83±0.44 and among patients without arrhythmia was 9.84±0.72. There was no significant difference between the two groups. Yucel colkesen et al in 2007, found out that MPV is significantly raised in patients with paroxysmal atrial fibrillation. However the present study did not show any statistical correlation between arrhythmia and MPV. The MPV was compared among patients who survived without complications and those with complications. The mean was 9.62±0.71 and 10.09±0.54 respectively. The MPV in patients with complication was found to be significantly different and higher than that of the patients without complications. Tagleri N , Saia F et al in 2011, in their study found out that higher MPV during the admission time was associated with complications in acute coronary syndrome. They claimed that MPV could be used as an important tool for risk stratification in acute coronary events. Rosa A Lopez et al in 2012 , in their study ,concluded that elevated MPV determined in the first

24hrs following admission was associated with a poorer in- hospital prognosis due to an increase in mortality. In the present study also elevated MPV was associated with an increased incidence of complications. The Mean Platelet count was compared among patients who died and those who did not . The mean was 10.53±0.35 and 9.73±0.65 respectively in the 2 groups. The MPV in patients who died was significantly different and higher than the patients who did not die. Thus similar to the observations of Rosa A Lopez et al, the present study also showed an increased mortality associated with higher MPV. The same observations were made by Hendra J et al(1998), Osuna et al (1998) and Martin et al (1991).

LIMITATIONS OF THE STUDY

1. Serial monitoring of increase in MPV was not assessed.

   This might have given a better insight into the nature of progression in those who developed complications.
2. The follow up period was only seven days. Prolonged follow up analysis might have resulted in a valid conclusion regarding prognostic implications
3. Economical constraints has led to the limited sample size. Future studies with larger sample size are needed.

CONCLUSION

- MPV was significantly elevated in Myocardial infarction group (9.84±0.67 fl) when compared to Unstable angina (9.07±0.77fl) and control groups(6.85±0.73fl)
- In the MI group the mean platelet count was 141800±63350 and the values ranged from 75000 to 310000, in the Unstable angina group the mean was 138243±61436 and the values ranged from 80000 to 340000 and finally in the Control group the mean was 230800±56856 and the values ranged from 120000 to 340000. Platelet count was significantly lower in MI and unstable angina group when compared to control group.
- MPV of 8.8 fl has 91.11% sensitivity and 62.12% specificity in detecting MI when compared to Trop –T
- No significant difference was observed in MPV between the age groups, but MPV was found to increase by 0.193 as age advances by 1yr as evidenced by β coefficient for age multiple linear regression analysis.

- MPV was found to be gender independent
- MPV in acute coronary syndrome was found to be independent of smoking and diabetes mellitus.
- The study showed that an increase in age, total cholesterol or random blood sugar by one unit will increase the MPV by 0.193, 0.183 and 0.355 respectively as evidenced by the beta coefficients
- MPV was found to be significantly elevated in hypertensives (9.42±1.03fl), when compared to non- hypertensives(8.43±1.44fl)
- MPV was found to influence the short term outcome after MI

  The MPV in patients with Complications(10.09±0.54 fl) was significantly different and higher than the patients without complications(9.62±0.71fl). So patients with higher MPV may be expected to manifest with complications in MI

  - MPV was significantly elevated in patients with

  lower ejection fraction. So a higher admission time MPV,

  can predict a lower ejection fraction in MI .

  - MPV was not related to the occurrence of arrhythmia in MI
- The MPV in patients who died(10.53±0.35 fl) was significantly different and higher than the patients who did not die. Hence larger MPV was found to predict the mortality

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ANNEXURE I

PROFORMA

Case No :

Name : Occupation:

Age : IP No :

Sex :

Date Of Admission :

Date Of Discharge / Death:

HISTORY

Time of onset of chest pain:

Time of admission :

Previous MI : Yes/ No

Previous Unstable angina : Yes/ No

Smoking :Yes/ No

Systemic Hypertension : Yes/No, if Yes , under regular treatment ? Yes/ No

Diabetes mellitus :Yes/No, if Yes , under regular treatment ? Yes/ No

EXAMINATION

Pulse:

Blood pressure:

S3 : Yes/ No

JVP elevation: Yes/No Killip class: I II III IV

Basal crackles : Yes/ No

INVESTIGATIONS:

Blood sugar : Hb: TC: DC:

Blood urea : ESR:

Serum creatinine : Peripheral smear:

Serum Total cholesterol : Others:

Troponin T card test : Positive / Negative

Mean platelet Volume :

Platelet count :

ECG :

ECHO

1. RWMA : Yes/ No, if yes which wall?
2. Ejection fraction :
3. Diastolic dysfunction :
4. Clot :

Diagnosis :

<u>OUTCOME</u>

Survived without complications:

with complications :

Death

MASTER CHART

S.No	NAME	SEX	AGE	MI	DM	HTN	SMOKING	RBS	T.Chol	MPV	Platelet count	Arrhythmia	Death	EF	No compl
1	Ganeshan	1	78	1	2	1	1	136	184	10.3	100000	2	2	50	1
2	kuppusamy	1	57	1	1	2	2	238	220	9.6	90000	1	2	40	2
3	Thankamani	1	45	1	2	1	2	126	188	10.4	120000	2	2	40	1
4	Arumugham	1	45	1	2	2	1	130	150	9.6	100000	2	2	54	1
5	vasu	1	47	1	2	1	1	110	240	11	88000	2	2	40	1
6	Abdul latheef	1	63	1	1	2	1	310	178	10.1	88000	2	2	40	1
7	Thomas	1	67	1	2	1	1	130	180	8.8	140000	2	2	65	1
8	Kanagambika	2	72	1	1	1	2	240	200	10.2	80000	2	2	36	2
9	Perumal	2	65	1	1	1	2	190	168	10	90000	2	1	30	2
10	Murugaiyyan	1	63	1	1	1	1	240	177	10.1	120000	2	2	30	2
11	krishnamoorthy	1	60	1	2	1	1	130	140	8.6	130000	2	2	50	1
12	Amsammal	2	78	1	2	2	2	140	150	8.9	100000	2	2	36	2
13	Arumugham	1	60	1	2	1	2	120	170	10	120000	1	2	40	2
14	Joseph	1	55	1	2	2	1	140	180	10.4	80000	2	2	40	1
15	Sellachi	2	50	1	1	2	2	190	240	10	80000	2	2	30	2
16	Ramani	2	64	1	2	1	2	140	220	8.6	100000	2	2	46	1
17	Kannan	1	52	1	2	1	1	130	200	10.4	75000	2	1	20	2
18	Thyagarajan	1	57	1	2	2	1	102	200	9	80000	2	2	46	1
19	Arokyasamy	1	65	1	2	1	1	110	156	10.2	200000	2	2	40	1
20	Chandravel	1	35	1	1	1	2	180	190	9.8	300000	2	2	56	1
21	Chelladurai	1	40	1	2	2	1	120	160	10.6	310000	2	2	52	1
22	Sundaram	1	60	1	1	2	2	210	226	11	120000	2	2	36	2
23	Mohammed sharif	1	48	1	2	1	1	130	240	10.1	140000	2	2	46	1
24	Muthuraja	1	30	1	2	1	1	120	230	9	180000	2	2	50	1
25	Karuppaiyya	1	30	1	1	1	1	140	200	10.6	90000	2	1	20	2
26	Uthrapathi	1	42	1	2	1	2	136	190	9	200000	2	2	56	1

27	Sahayaraj	1	50	1	2	1	1	140	156	9.4	160000	2	2	40	1
28	Anbazhagan	1	60	1	1	1	2	166	210	10.4	100000	2	2	40	2
29	Joseph raj	1	72	1	1	1	2	170	190	9.8	240000	2	2	44	2
30	Ranganathan	1	62	1	1	1	2	180	190	9.8	90000	1	2	34	2
31	Elangovan	1	33	1	2	1	2	130	200	9	200000	2	2	44	1
32	Mariyammal	2	58	1	1	2	2	260	220	10.2	100000	1	2	40	2
33	Vembu	2	28	1	2	2	2	130	240	10.1	200000	2	2	66	1
34	Pankajam	2	75	1	2	1	2	130	180	11	100000	2	1	26	2
35	Anjammal	2	65	1	1	1	2	140	160	10	100000	2	2	40	1
36	Devaki	2	65	1	2	2	2	120	150	9	200000	2	2	46	1
37	Asokan	1	40	1	2	1	1	110	190	9.4	100000	2	2	70	1
38	Paulraj	1	53	1	2	1	1	130	190	10.4	120000	1	1	36	2
39	Shakthi	2	40	1	1	2	2	268	200	10.8	200000	2	1	24	2
40	Thambaiyya	1	69	1	2	2	1	146	186	10	200000	2	2	72	1
41	Vasantha	2	60	1	1	2	2	190	212	9.6	150000	1	2	44	2
42	Nagendran	1	58	1	1	1	1	230	180	10.1	100000	1	2	40	2
43	Kunjuppillai	1	60	1	2	2	2	140	160	8.6	200000	2	2	76	1
44	Shakthi	1	55	1	2	2	1	136	200	10	300000	2	2	38	2
45	Govindasamy	1	52	1	2	1	1	120	190	9	200000	1	2	64	2

MYOCARDIAL INFARCTION GROUP

SEX- 1→ Male, 2→ Female

Other variables

1→ yes, 2→ No

UNSTABLE ANGINA GROUP

S.No	NAME	SEX	AGE	UNSTABLE ANGINA	DM	HYPERTENSION	SMOKING	RBS	T.Chol	MPV	PLATELET COUNT
1	gopalasamy	1	76	1	2	1	1	140	210	9.6	90000
2	veeraguru	1	50	1	2	2	1	130	186	7	240000
3	Ramakaya	1	67	1	1	2	2	176	200	8.8	240000
4	Anjam	1	48	1	2	1	2	120	210	8.8	200000
5	venkitachalam	1	60	1	2	1	2	110	190	9.6	100000
6	Muthaiyya	1	40	1	2	1	2	120	186	9.8	200000
7	Boss	1	52	1	1	2	2	186	200	10.4	110000
8	Thavapandiyan	1	42	1	2	1	1	136	190	10.6	140000
9	Ramalingam	1	35	1	2	2	2	120	160	7.8	340000
10	povaliyan	1	55	1	2	1	1	140	210	9.6	90000
11	palanimuthu	1	37	1	2	2	2	110	180	8.8	260000
12	Appaviraja	1	65	1	2	1	2	120	180	9.1	200000
13	Mohamed ismail	1	71	1	1	2	2	178	200	10	100000
14	Arokyasamy	1	62	1	2	1	2	110	240	10	100000
15	Rajandran	1	55	1	2	2	2	86	170	9.2	90000
16	Muthukrishnan	1	60	1	2	2	2	90	160	9	88000
17	George	1	39	1	2	1	1	110	240	8.8	140000
18	Muthaiyan	1	49	1	2	2	2	126	200	7.8	280000
19	Durairaj	1	32	1	2	2	2	130	188	9.4	100000
20	Nazeemudheen	1	45	1	2	2	2	140	190	8.8	120000
21	Sreenivasan	1	50	1	1	1	1	220	240	9	130000
22	Lenin Raj	1	65	1	2	1	1	130	190	8.6	120000
23	Kam Raj	1	45	1	2	2	2	140	196	8	140000
24	Malayan	1	40	1	2	1	1	110	200	10	100000

25	Arumugham	1	60	1	2	2	1	120	188	10	120000
26	Subramanyan	1	30	1	2	2	2	110	190	9.8	100000
27	Sathyamoorthy	1	80	1	2	1	1	110	170	9.6	100000
28	Muthu	1	64	1	2	2	2	120	180	8.8	160000
29	Sekhar	1	40	1	1	1	2	230	200	9	100000
30	Rajeshwari	2	77	1	2	1	2	130	196	9.4	90000
31	Rukmini	2	64	1	2	1	2	140	190	9	200000
32	Annapoorna	2	38	1	1	2	2	240	200	9.6	100000
33	Duraiyammal	2	70	1	1	2	2	270	200	9.4	110000
34	Lakshmi	2	35	1	1	2	2	190	210	9	160000
35	Sumathy	2	40	1	2	1	2	110	200	8.8	100000
36	Dhanalakshmi	2	65	1	1	2	2	130	170	8.1	80000
37	Thaiyyal nayaki	2	55	1	2	1	2	126	188	8.6	100000
38	Yasodhai	2	50	1	1	2	2	100	160	7.4	120000
39	Dhanakodi	2	60	1	2	2	2	128	170	8.8	90000
40	Palani	2	67	1	2	1	2	110	180	9	100000
41	Neelamagham	2	68	1	2	1	2	126	270	9.4	120000

SEX- 1→ Male, 2→ Female

Other variables

1→ yes, 2→ No

CONTROL GROUP

S.No	NAME	SEX	AGE	DIABETES	Hypertension	SMOKING	SUGAR	CHOLESTEROL	MPV	PLATELET COUNT
1	selvi	2	40	2	2	2	125	160	6	240000
2	pavanambal	2	45	1	2	2	165	160	7.8	300000
3	ramu	1	68	2	2	2	125	178	7	300000
4	raghav	1	40	2	2	2	140	180	8	200000
5	anbujam	2	55	2	1	1	135	168	6	200000
6	veeraiyyan	1	54	2	1	1	136	169	6.6	210000
7	kumar	1	37	2	2	2	146	230	6.5	120000
8	kaviyarasu	1	45	2	2	2	120	160	6.2	230000
9	kathirvel	1	41	2	2	2	100	190	7	300000
10	nageenthran	1	42	1	2	2	130	188	8.4	340000
11	kala	2	55	2	2	2	120	156	6	310000
12	jaffer	1	66	1	1	2	145	169	6.2	200000
13	noorbeevi	2	56	2	2	2	140	166	6.4	210000
14	kasthuri	2	33	1	2	2	160	188	6.6	150000
15	kathirvel	1	32	2	2	2	136	182	7.3	160000
16	lakshmi	2	66	1	2	2	180	163	7	190000
17	thirunavakarasu	1	58	2	2	2	120	194	8.1	230000
18	pushparaj	1	60	2	2	2	130	168	7.2	240000
19	maithili	2	35	1	2	2	180	166	6.6	200000
20	munusamy	1	50	2	2	2	98	172	6	190000
21	venugopal	1	51	2	2	2	90	178	6.1	200000
22	sardar	1	52	2	2	2	136	174	6.3	240000
23	manu	1	60	2	2	1	130	165	7	200000
24	pichaiyammal	2	44	2	2	2	120	176	7	300000
25	fathima	2	45	2	2	2	130	180	8	310000

ANNEXURE III

ABBREVIATIONS

ACS - Acute Coronary Syndrome

LDL - Low Density Lipoprotein

MPV - Mean Platelet Volume

HDL - High Density Lipoprotein

NO - Nitric Oxide

PF4 - Platelet Factor 4

ADP - Adenosine Di Phosphate

ATP - Adenosine Tri Phosphate

GTP - Guanosine Tri Phosphate

TXA2 - Thromboxane A2

STEMI- ST Elevation Myocardial Infarction

MI - Myocardial Infarction

ECG - Electro Cardio Gram

Std. - Standard

Sig. - Significance

TGF - Transforming Growth Factor

Df - Degree of Freedom

DM -Diabetes Mellitus

HTN - Hypertension

RBS - Random Blood Sugar

T. Chol - Total Cholesterol

EF - Ejection Fraction

No Comp- No Complication